Electronic Supplementary Information

Modular Triazine-based Carborane-containing Carboxylic Acids – Synthesis and Characterisation of Potential Boron Neutron Capture Therapy Agents Made of Readily Accessible Building Blocks

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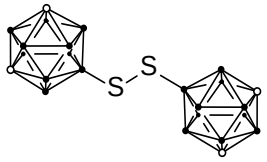
Experimental Section: Details including references are given in the main text.

1. Synthesis of 1,2-di(1,7-dicarba-*closo*-dodecaboran-9-yl)disulfane (1)



1

The following synthesis is based on the procedure of Zakharkin *et al*.[1]

A 500 mL two-necked round bottom flask equipped with a dropping funnel and a condenser was charged with 20.15 g (139.7 mmol, 2.00 eq.) 1,7-dicarba-*closo*-dodecaborane(12) and 18.75 g (140.6 mmol, 2.02 eq.) anhydrous aluminium chloride and was subsequently evacuated and purged with nitrogen three times. To this mixture, 250 mL of dry dichloromethane were added and the solution was cooled to 0 °C. A solution of 5.60 mL (9.46 g, 70.1 mmol, 1.00 eq.) disulfur dichloride in 20 mL dry dichloromethane was transferred to the dropping funnel and added dropwise at 0 °C to the mixture of 1,7-dicarba-*closo*-dodecaborane(12) and $AlCl_3$ in dichloromethane. After addition, the reaction mixture the suspension was left to warm up to room temperature and then stirred for six hours at reflux conditions and one more night at room temperature. After the reaction was finished, the mixture was poured onto crushed ice. The organic layer was separated from the aqueous one and the aqueous layer was extracted once with 20 mL dichloromethane. Afterwards the combined organic layers were washed once with 100 mL distilled water, dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. The crude product **1** was about 26.05 g with some impurities; 20.57 g were used for the synthesis of compound **2** and the remaining 5.48 g were purified by column chromatography (chloroform/*n*-hexane, 1:1, v/v). 2.81 g of **1** (8.02 mmol, 11.4%, R_f = 0.51, chloroform/*n*-hexane, 1:1, v/v) were obtained as a slightly yellow solid. T_m: 322-324 °C (methanol). Elemental analysis: $C_4H_{22}B_{20}S_2$, calculated (%): C 13.70, H 6.33; found (%): C 13.69, H 6.38. IR (KBr): $\tilde{\nu}$ = 3422 (w), 3046 (m), 2601 (s), 1642 (w), 1310 (s), 1239 (s), 1186 (m), 1154 (s), 1062 (m), 1031 (w), 987 (s), 947 (s), 915 (w), 859 (s), 825 (w), 808 (w), 755 (m), 722 (m), 675 (w), 624 (w), 586 (w), 523 (w) cm^{-1}. ^1H NMR (400.16 MHz, chloroform-d_1): δ = 1.45 – 3.40 (m, br[a],[1] 18 H, $B_{10}H_9$), 2.97 (s, br, 4 H, CH) ppm. $^{13}C\{^1H\}$ NMR (100.63 MHz, chloroform-d_1): δ = 53.9 (s, CH) ppm. $^{11}B\{^1H\}$ NMR (128.38 MHz, chloroform-d_1): δ = –20.4 (s, br, 2 B), –17.6 (s, 2 B), –14.0 (s, 4 B), –13.0 (s, 4 B), –9.7 (s, 2 B), –6.2 (s, 4 B), –1.5 (s, 2 B, BS) ppm. ^{11}B NMR (128.38 MHz, chloroform-d_1): δ = –20.4 (d, $^1J_{BH}$ = 182 Hz, 2 B), –17.6 (d, $^1J_{BH}$ = 182 Hz, 2 B), –13.5 (m, 8 B), –9.7 (d, $^1J_{BH}$ = 153 Hz, 2 B),

[1] NMR signals that appear as broad overlapping signals with the shape of a multiplet are described as br[a].

–6.2 (d, $^{1}J_{BH}$ = 166 Hz, 4 B), –1.5 (s, 2 B, BS) ppm. ESI MS: positive mode, $C_4H_{23}B_{20}S_2$, m/z calculated: 351.3, found: 351.3 (35%, $[M+H]^+$).

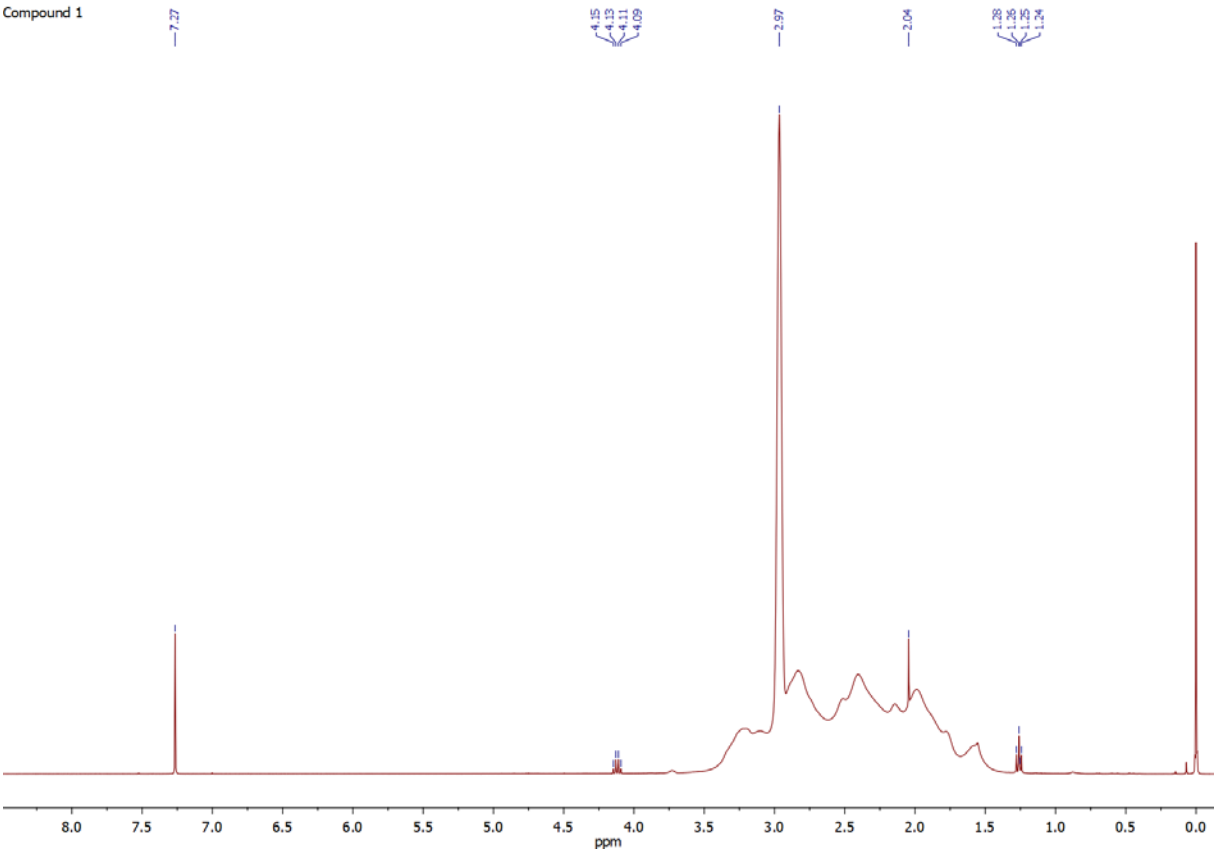


Figure S1: ^{1}H NMR spectrum of compound **1** with some minor impurities of ethyl acetate.

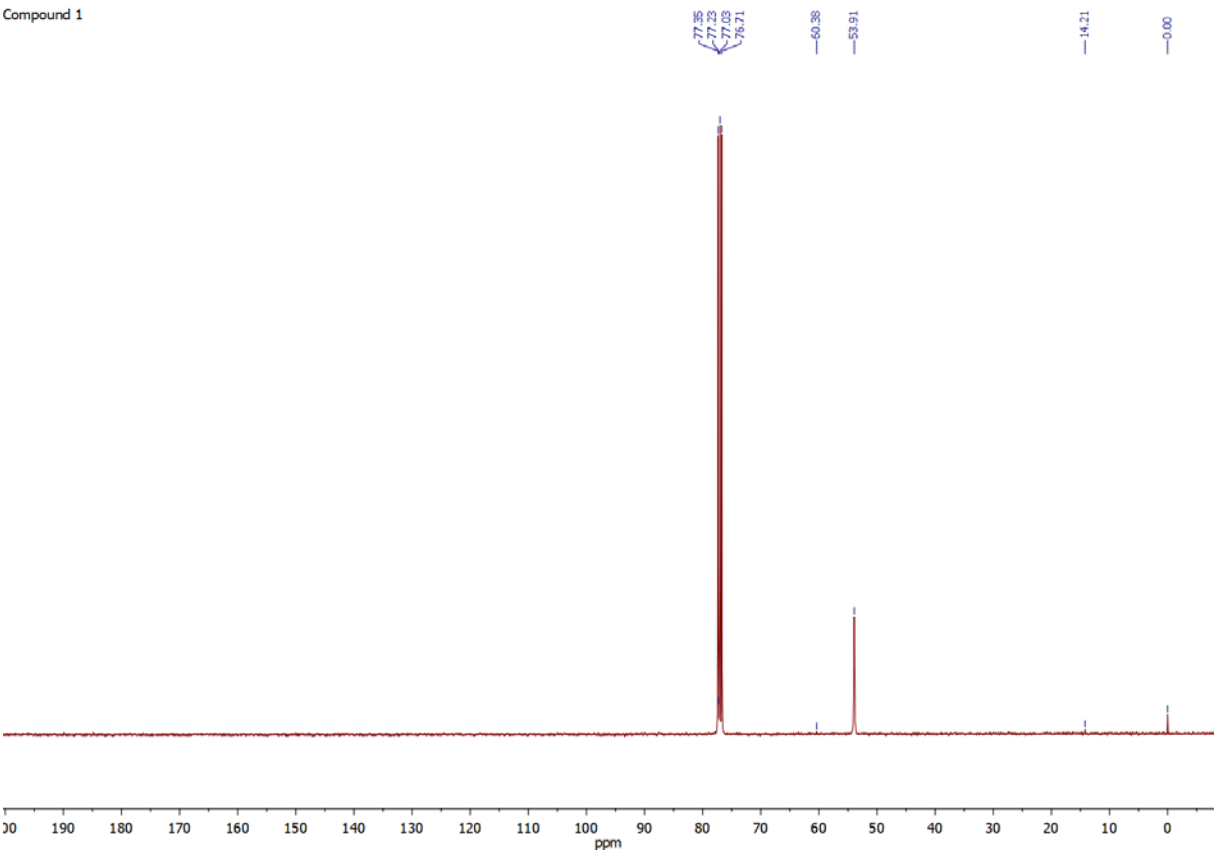


Figure S2: $^{13}C\{^{1}H\}$ NMR spectrum of compound **1** with some minor impurities of ethyl acetate.

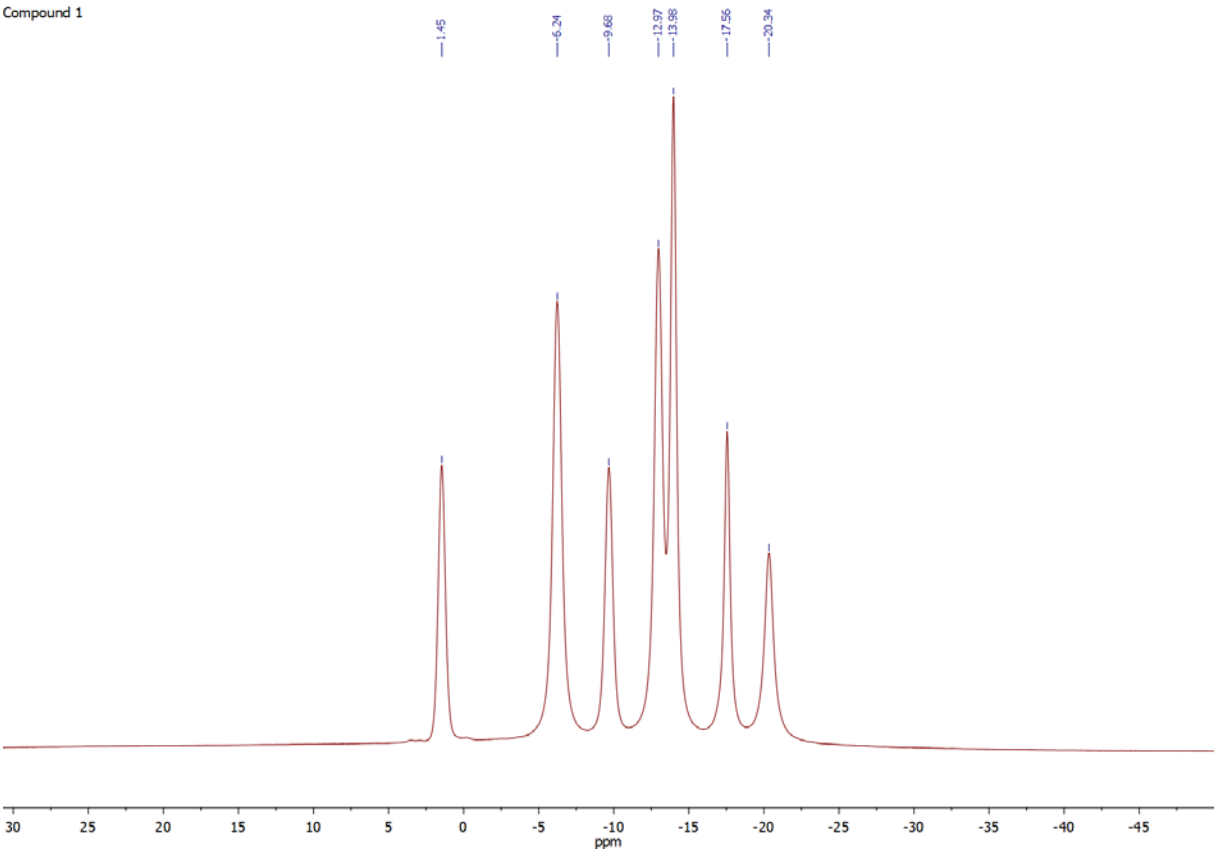


Figure S3: $^{11}B\{^{1}H\}$ NMR spectrum of compound **1**.

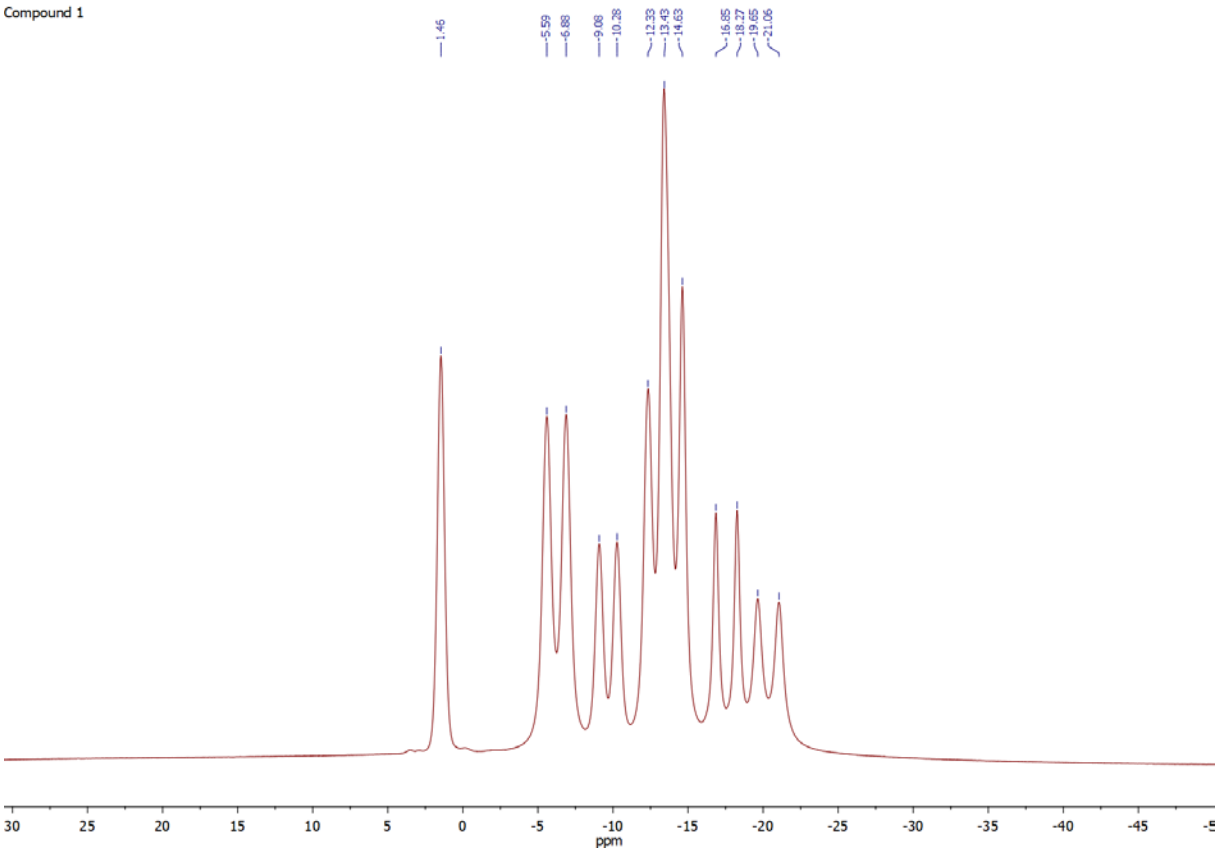


Figure S4: ^{11}B NMR spectrum of compound **1**.

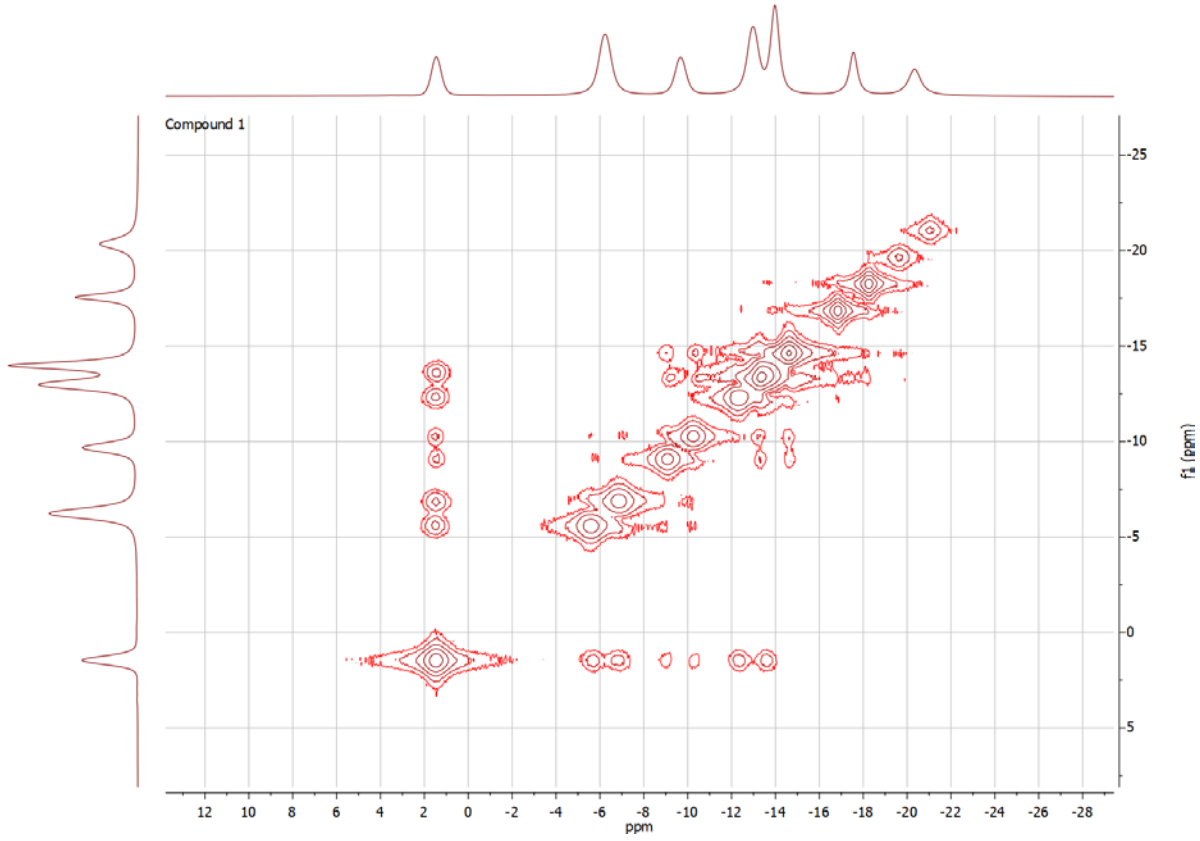


Figure S5: ^{11}B-^{11}B-COSY NMR spectrum of compound **1**.

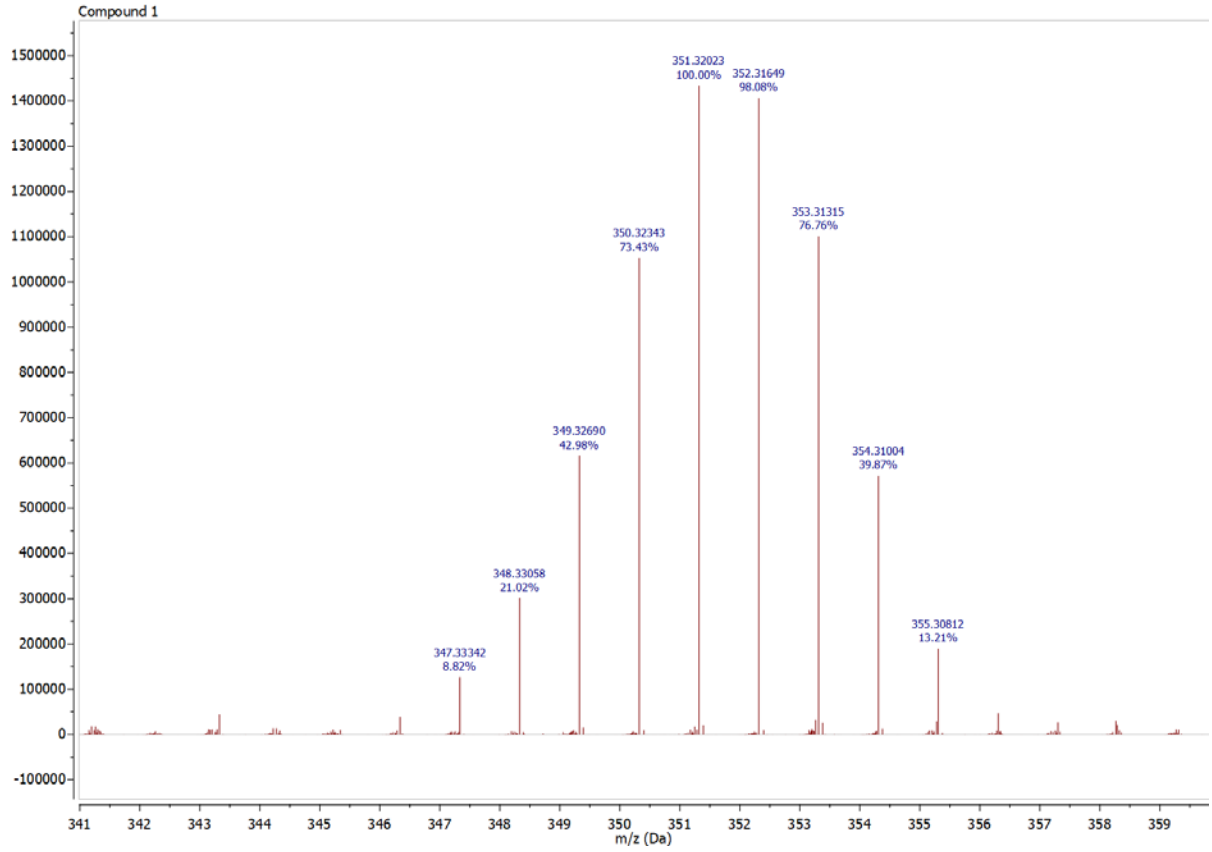


Figure S6: ESI MS (positive mode) of compound **1**.

2. Crystallographic data of 1

Empirical formula	$C_4H_{22}B_{20}S_2$	
Formula weight	350.53	
Temperature	130(2) K	
Wavelength	71.073 pm	
Crystal system	Trigonal	
Space group	$P3_1$	
Unit cell dimensions	a = 1354.93(3) pm	α = 90°
	b = 1354.93(3) pm	β = 90°
	c = 1783.48(5) pm	γ = 120°
Volume	2.8355 (2) nm^3	
Z	6	
Density (calculated)	1.232 Mg/m^3	
Absorption coefficient	0.266 mm^{-1}	
F(000)	1068	
Crystal size	0.20 x 0.20 x 0.10 mm^3	

Theta range for data collection	1.735 to 29.186°
Index ranges	–18 ≤ h ≤ 18, –18 ≤ k ≤ 17, –23 ≤ l ≤ 24
Reflections collected	26443
Independent reflections	8733 [R(int) = 0.0862]
Completeness to theta = 26.375°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.99289
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8733 / 1 / 469
Goodness-of-fit on F^2	1.003
Final R indices [I>2σ(I)]	R_1 = 0.0644, wR_2 = 0.1098
R indices (all data)	R_1 = 0.1216, wR_2 = 0.1294
Absolute structure parameter	–0.01(5)
Residual electron density	0.342 and –0.321 e·Å^{-3}

Comments: Structure solution with SHELXT-2014 (dual-space method). Anisotropic refinement of all non-hydrogen atoms with SHELXL-2018. All hydrogen atoms were calculated on idealised positions. Carborane carbon atoms could not be localised from a bond length and displacement parameter analysis. They are most likely disordered. The data indicate a C1–B3 disorder and the atoms C7 and C8 are most likely disordered over the entire C_2B_5 ring. However, the data has not been corrected for disordered atoms.

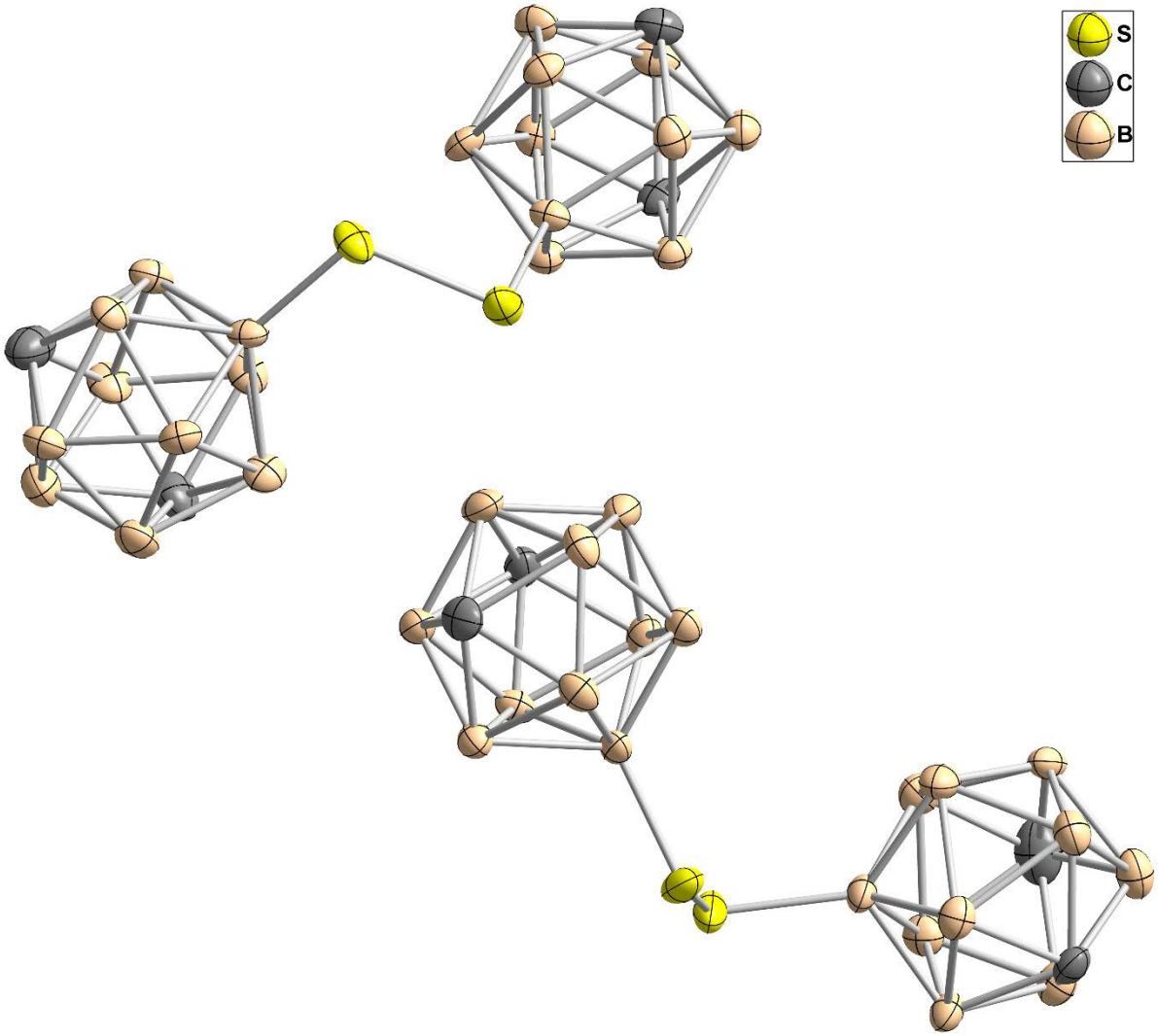
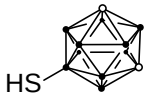


Figure S7: Molecular structure of **1**. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms are omitted for clarity.

3. Synthesis of 9-mercapto-1,7-dicarba-*closo*-dodecaborane(12) (2)



2

The following synthesis is based on the procedure of Zakharkin *et al*.[1]

A 500 mL two-necked round bottom flask equipped with a dropping funnel and a condenser was charged with 10.0 g (69.3 mmol, 1.00 eq.) 1,7-dicarba-*closo*-dodecaborane(12) and 9.28 g (69.6 mmol, 1.00 eq.) anhydrous aluminium chloride and was subsequently evacuated and purged with nitrogen three times. To this mixture, 200 mL of dry dichloromethane were added and the solution was cooled to 0 °C. A solution of 2.80 mL (4.73 g, 35.0 mmol, 0.51 eq.) disulfur dichloride in 35 mL dry dichloromethane was added to the dropping funnel and subsequently the mixture was added dropwise at 0 °C to the mixture of 1,7-dicarba-*closo*-dodecaborane(12) and $AlCl_3$ in dichloromethane. After addition, the reaction mixture the suspension was left to warm up to room temperature and then stirred for four hours at reflux conditions. The reaction progress was monitored by TLC (*n*-hexane/chloroform, 1:1, v/v). After the reaction was finished, the mixture was cooled to room temperature and poured onto crushed ice. The organic layer was separated from the aqueous one and the organic layer was washed two times with 100 mL distilled water. The organic layer was dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure.

The raw product was then placed in a 500 mL round bottom flask equipped with a condenser and dissolved in a mixture of 50 mL concentrated hydrochloric acid, 50 mL glacial acetic acid and 80 mL ethyl acetate. Then the mixture was stirred under reflux conditions. An excess of zinc powder was added to this solution in small portions over a period of two hours. After the reaction was finished, the mixture was cooled to room temperature and poured onto crushed ice. The resulting mixture was neutralised using sodium bicarbonate and sodium carbonate. After separation of the organic and aqueous layer the aqueous layer was extracted three times with 50 mL diethyl ether. The combined organic layers were washed once with 50 mL distilled water and then the organic layer was extracted four times with 50 mL 2.2 M potassium hydroxide solution. Subsequently, the combined basic aqueous layers were acidified with concentrated hydrochloric acid and the resulting precipitate was extracted three times with 50 mL diethyl ether. The combined organic layers were dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. 8.64 g (49.0 mmol, 70.7%) of **2** were isolated as a slightly pink crystalline solid. T_m = 185-188 °C (diethyl ether). Elemental analysis: $C_2H_{12}B_{10}S$, calculated (%): C 13.63, H 6.86; found (%): C 14.10, H 7.06. IR (KBr): $\tilde{\nu}$ = 3444 (s), 3050 (m), 3028 (s), 2965 (m), 2923 (w), 2853 (w), 2599 (s), 2361 (w), 2262 (w), 2098 (w), 1634

(m), 1460 (w), 1384 (w), 1262 (m), 1162 (m), 1128 (m), 1107 (m), 1067 (s), 1051 (s), 992 (s), 949 (s), 918 (w), 864 (s), 805 (s), 755 (m), 725 (s), 672 (m), 623 (w), 587 (w), 488 (w) cm^{-1}. ^{1}H NMR (400.16 MHz, acetone-d_6): δ = 0.70 (m, 1 H, SH), 1.44 – 3.39 (m, br[a], 9 H, $B_{10}H_9$), 3.75 (s, br, 2 H, CH) ppm. $^{13}C\{^{1}H\}$ NMR (100.63 MHz, acetone-d_6): δ = 56.5 (s, br, CH) ppm. $^{11}B\{^{1}H\}$ NMR (128.38 MHz, acetone-d_6): δ = –20.7 (s, 1 B), –17.3 (s, 1 B), –13.9 (s, 2 B), –12.4 (s, 2 B), –9.2 (s, 1 B), –6.0 (s, 2 B), –2.2 (s, 1 B, BS) ppm. ^{11}B NMR (128.38 MHz, acetone-d_6): δ = –20.7 (d, $^{1}J_{BH}$ = 182 Hz, 1 B), –17.3 (d, $^{1}J_{BH}$ = 182 Hz, 1 B), –13.2 (m, 4 B), –9.2 (d, $^{1}J_{BH}$ = 152 Hz, 1 B), –6.0 (d, $^{1}J_{BH}$ = 164 Hz, 2 B), –2.2 (s, 1 B, BS) ppm. ESI MS: negative mode, $C_2H_{11}B_{10}S$, m/z calculated: 175.1, found: 175.1 (12%, $[M-H]^-$).

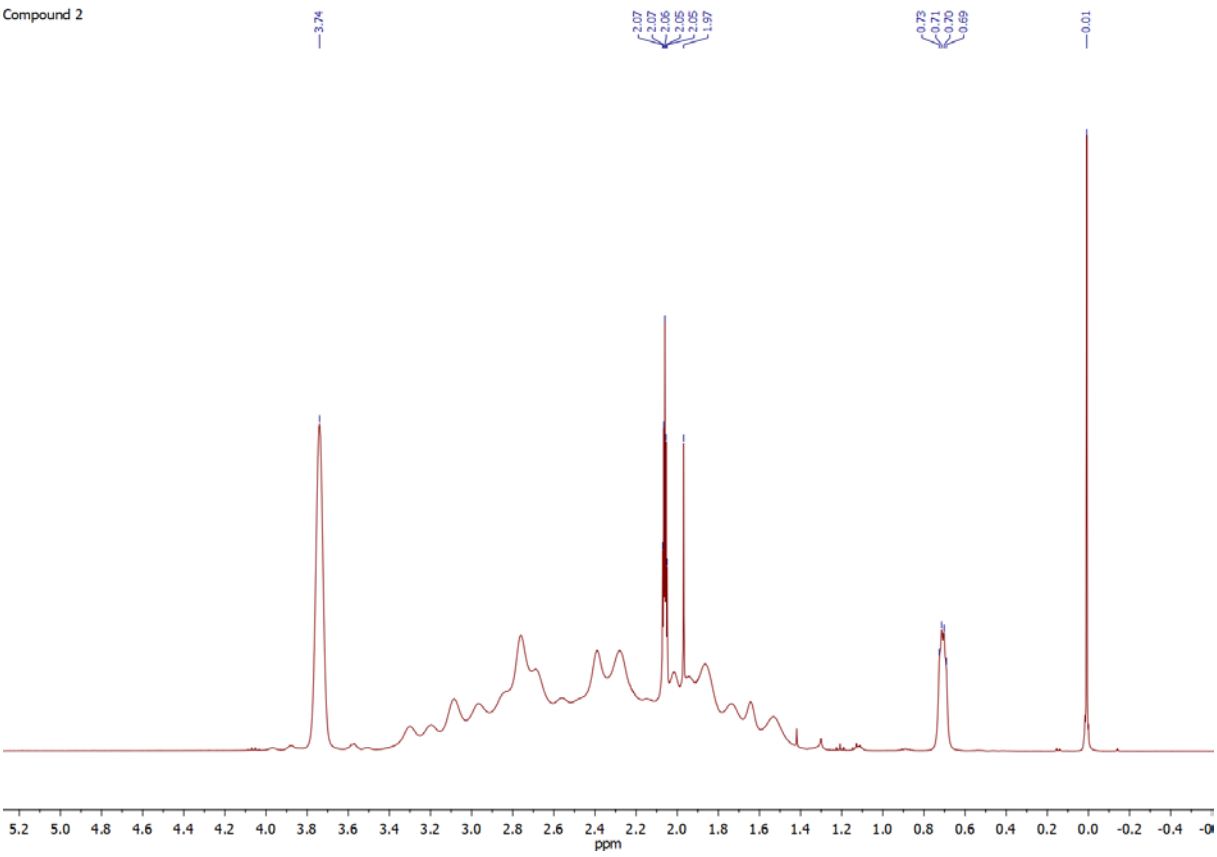


Figure S8: ^{1}H NMR spectrum of compound **2** with acetic acid as a minor impurity.

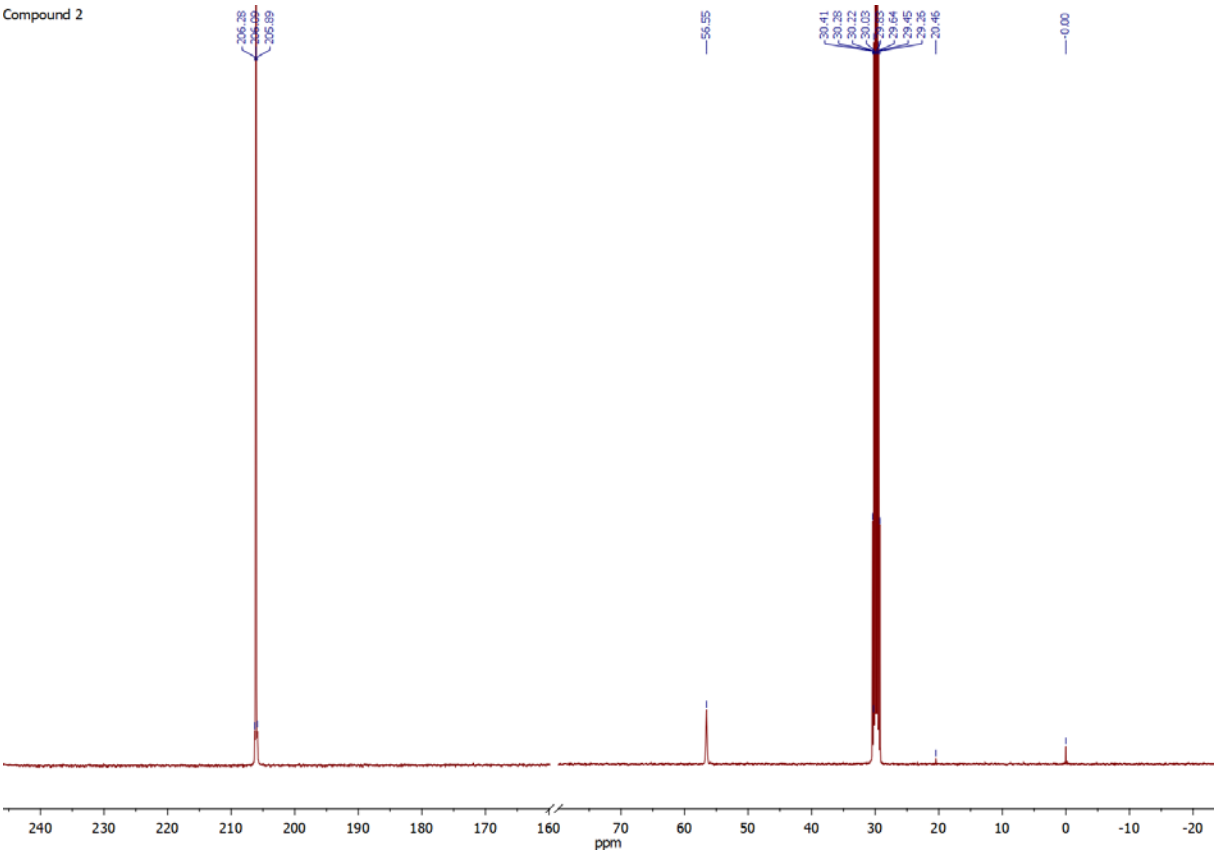


Figure S9: $^{13}C\{^{1}H\}$ NMR spectrum of compound **2** with acetic acid as a minor impurity.

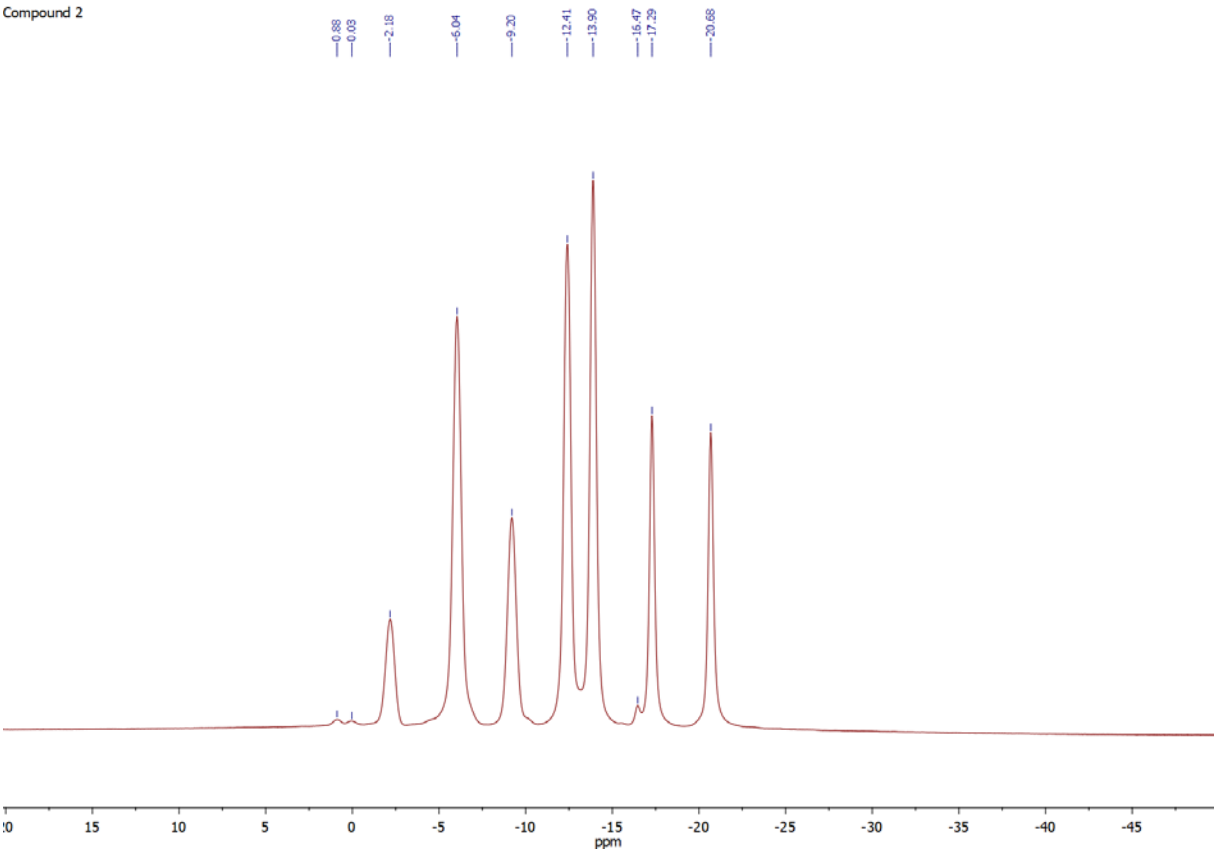


Figure S10: $^{11}B\{^{1}H\}$ NMR spectrum of compound **2**.

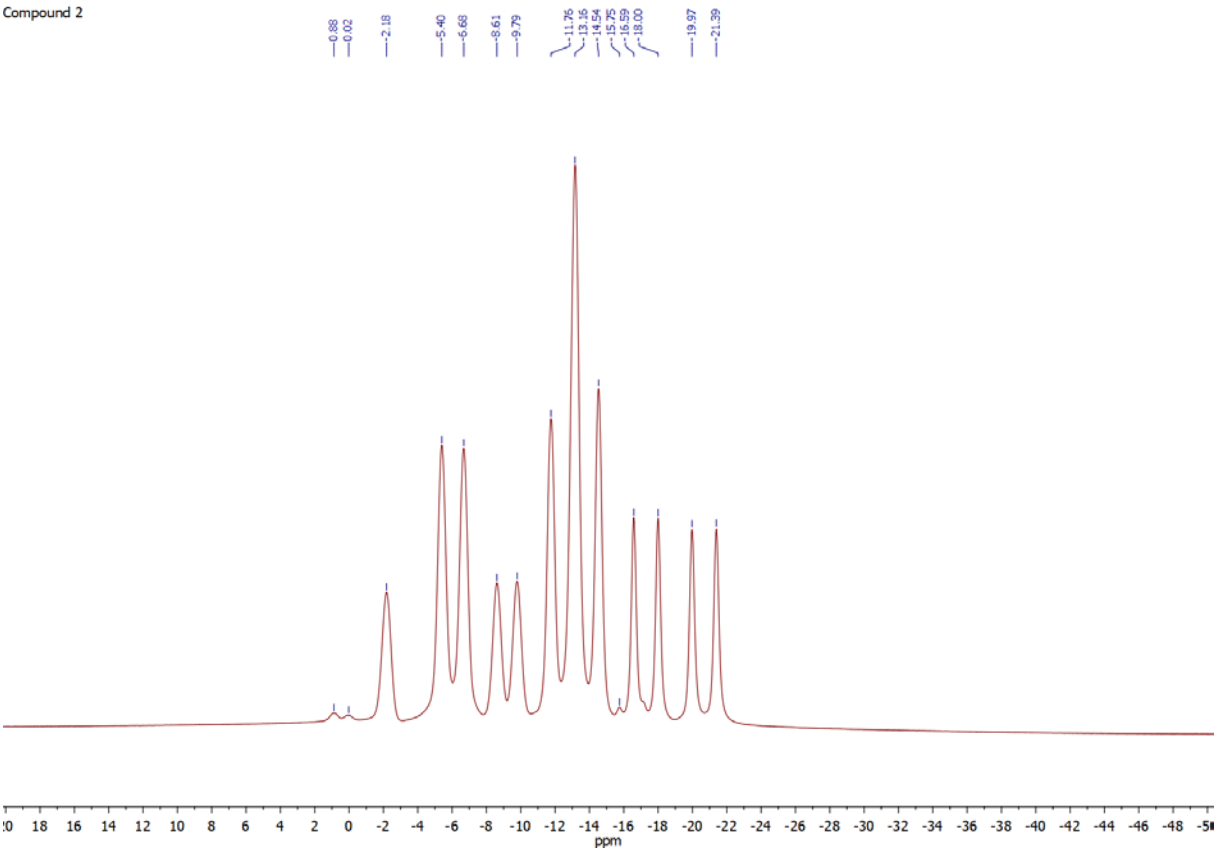


Figure S11: ^{11}B NMR spectrum of compound **2**.

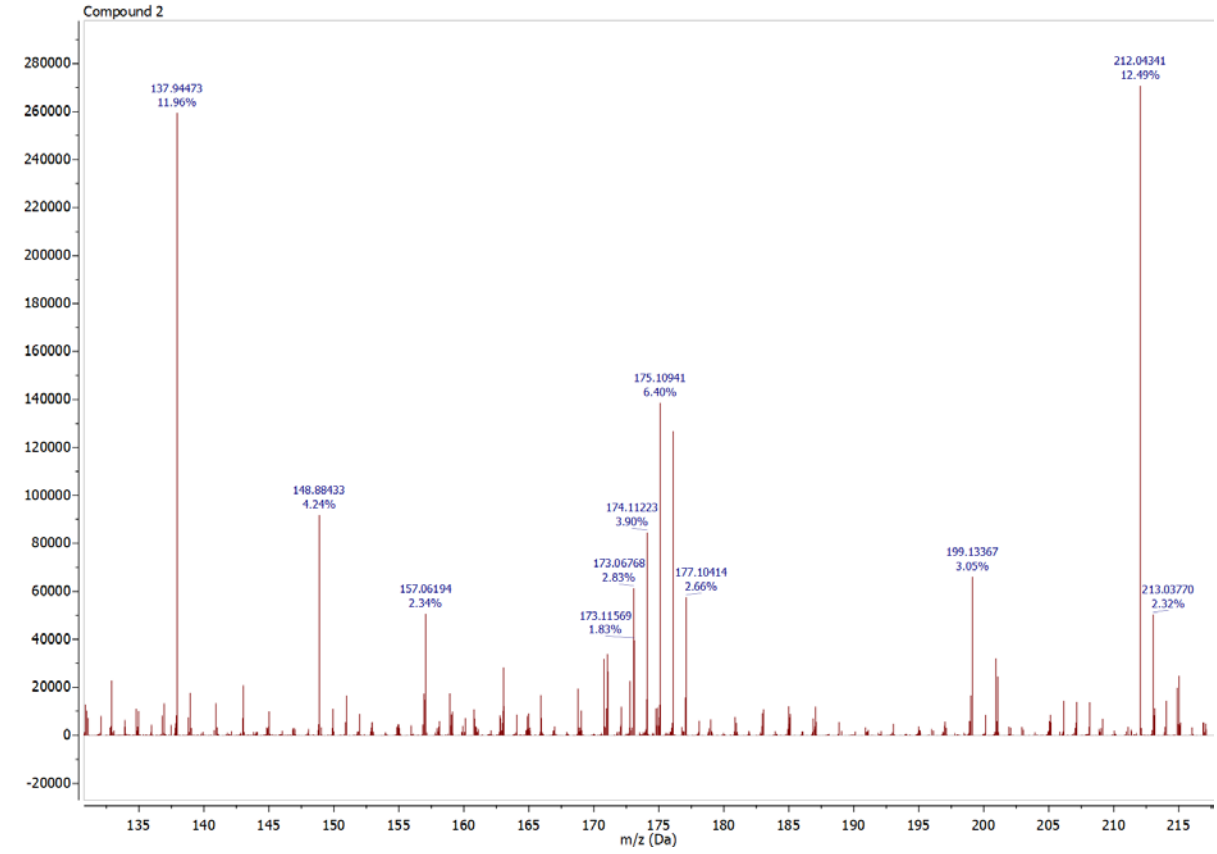


Figure S12: ESI MS (negative mode) of compound **2**.

4. Additional spectroscopic and crystallographic data of 2-chloro-4,6-bis(1,7-dicarba-*closo*-dodecaboran-9-ylthio)-1,3,5-triazine (3)

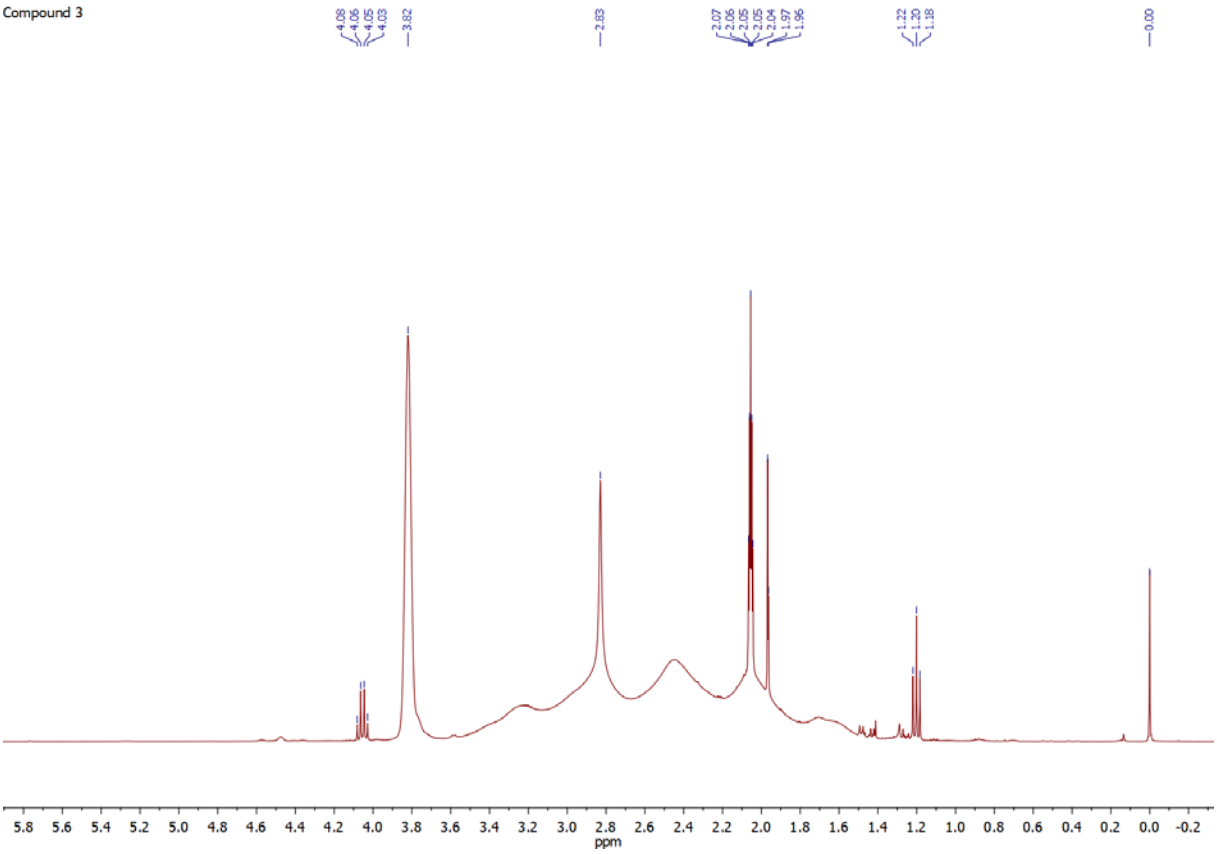


Figure S13: ^{1}H NMR spectrum of compound **3** with ethyl acetate and water as minor impurities.

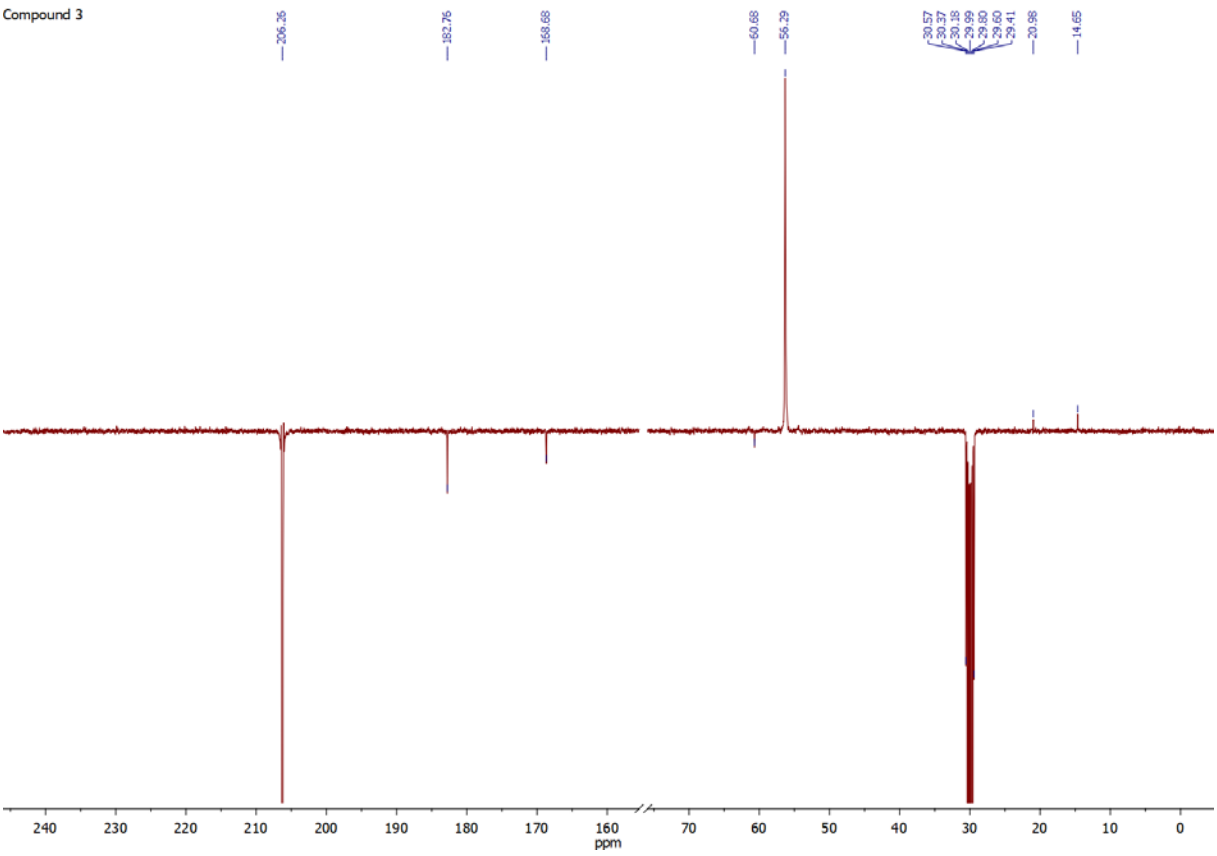


Figure S14: $^{13}C\{^{1}H\}$ NMR spectrum of compound **3** with ethyl acetate as a minor impurity.

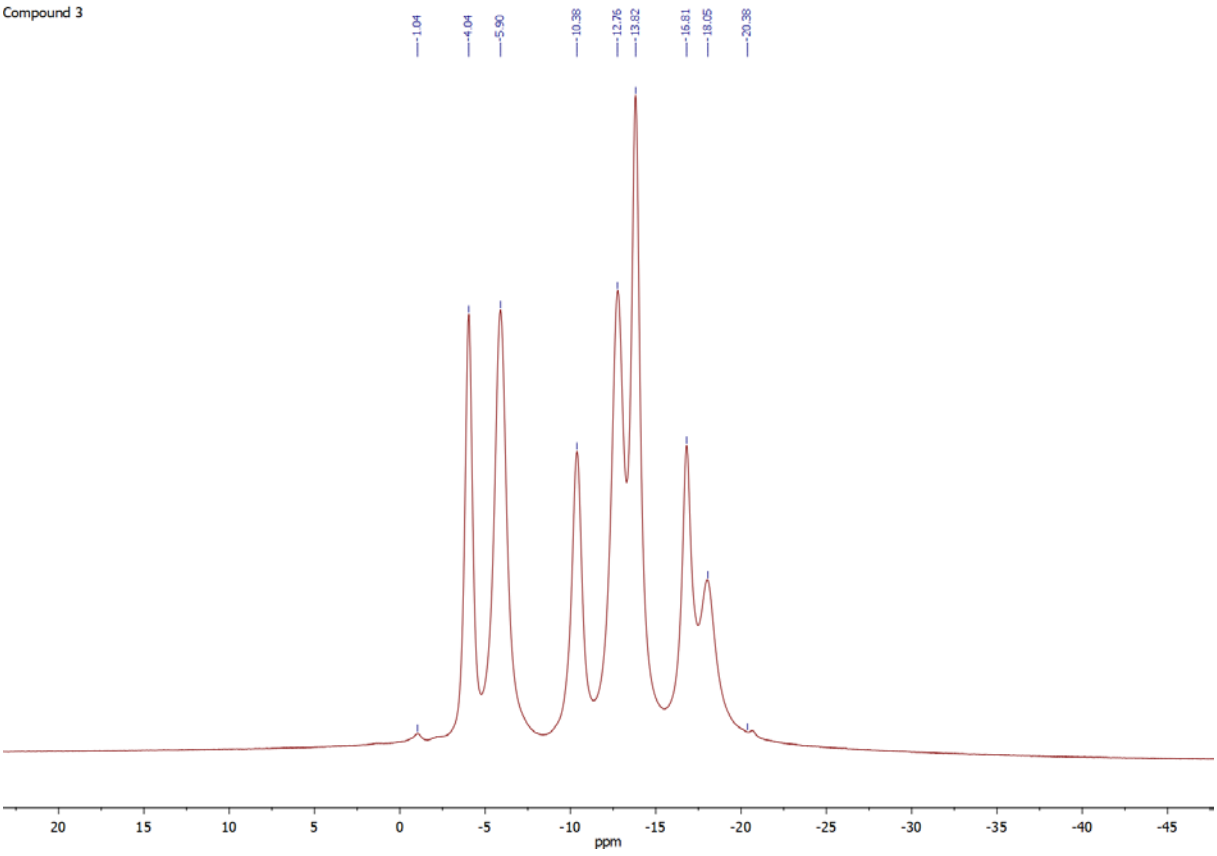


Figure S15: $^{11}B\{^{1}H\}$ NMR spectrum of compound **3**.

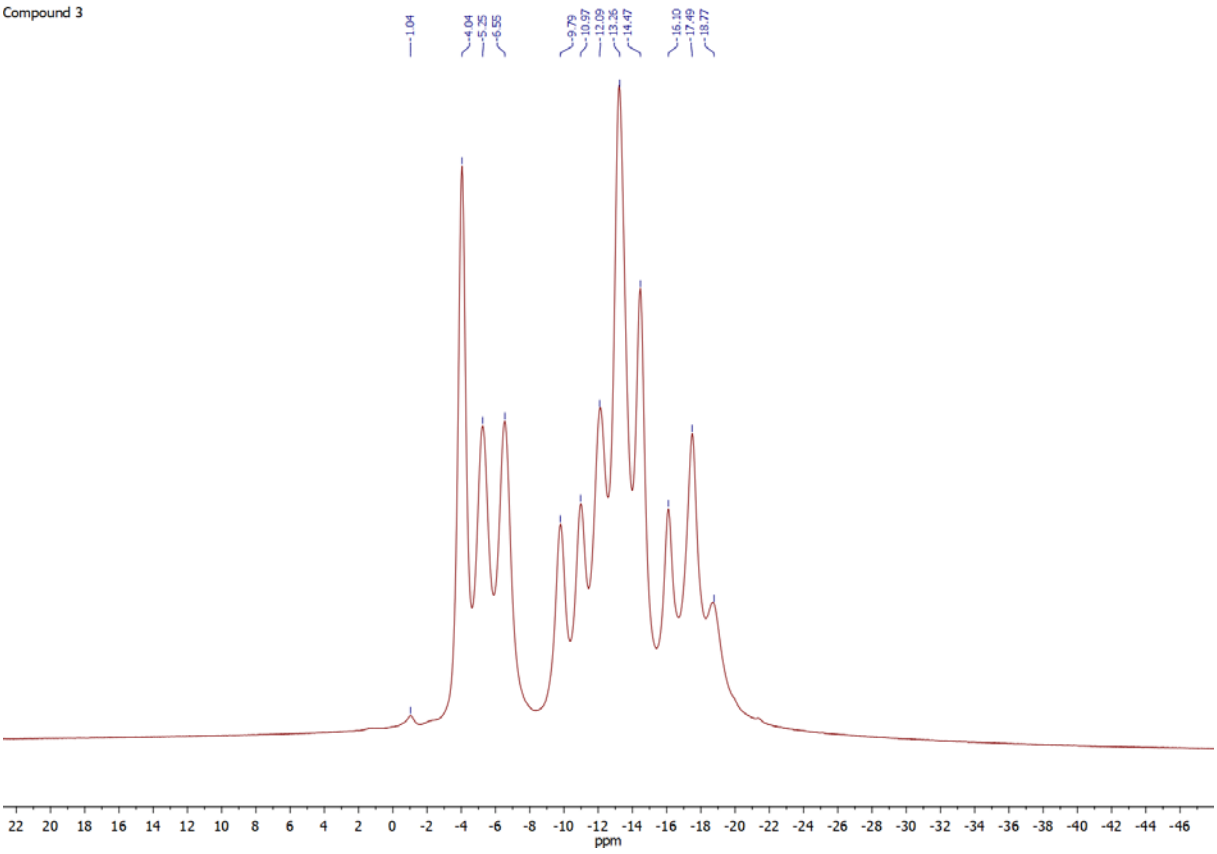


Figure S16: ^{11}B NMR spectrum of compound **3**.

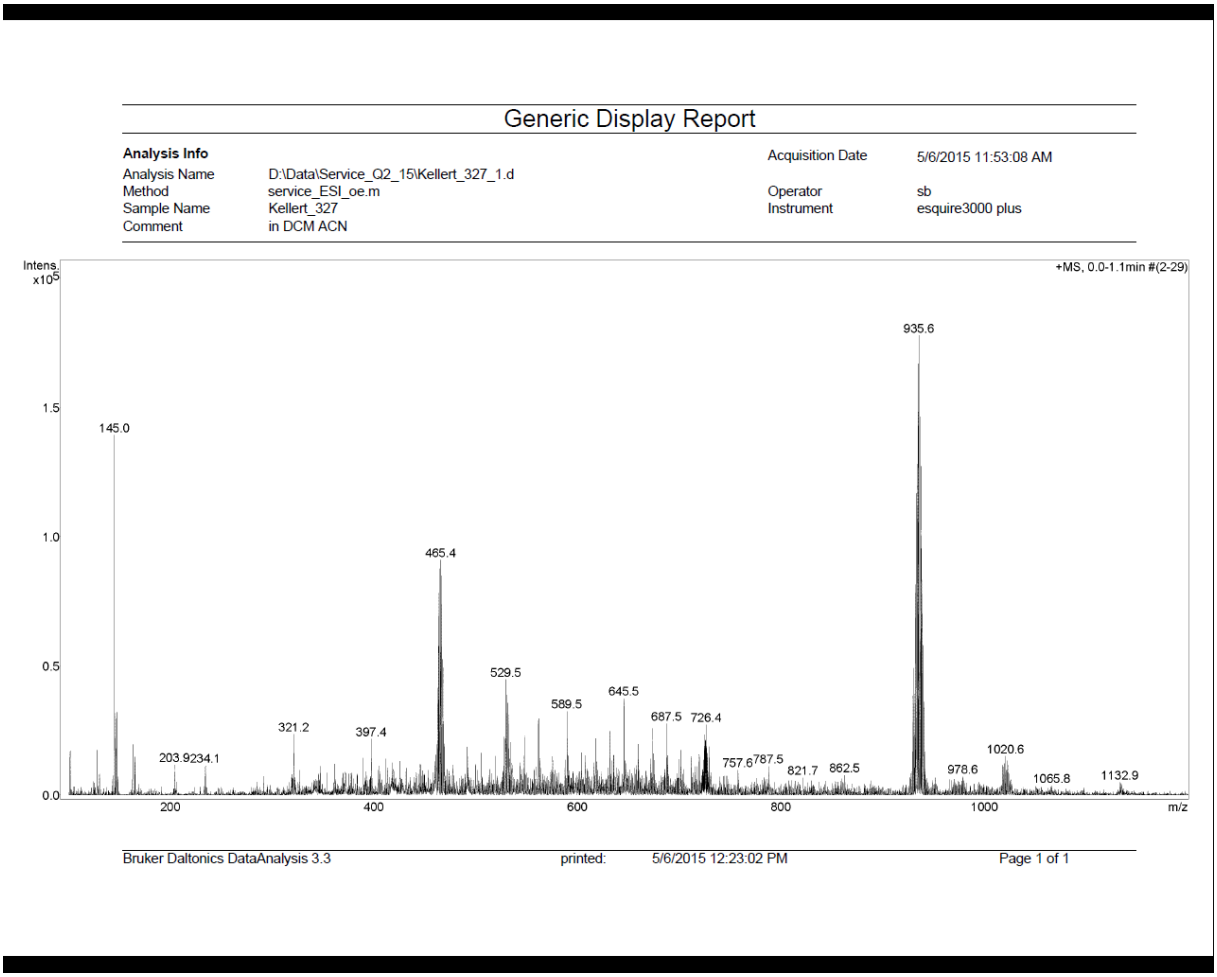


Figure S17: ESI MS (positive mode) of compound **3**.

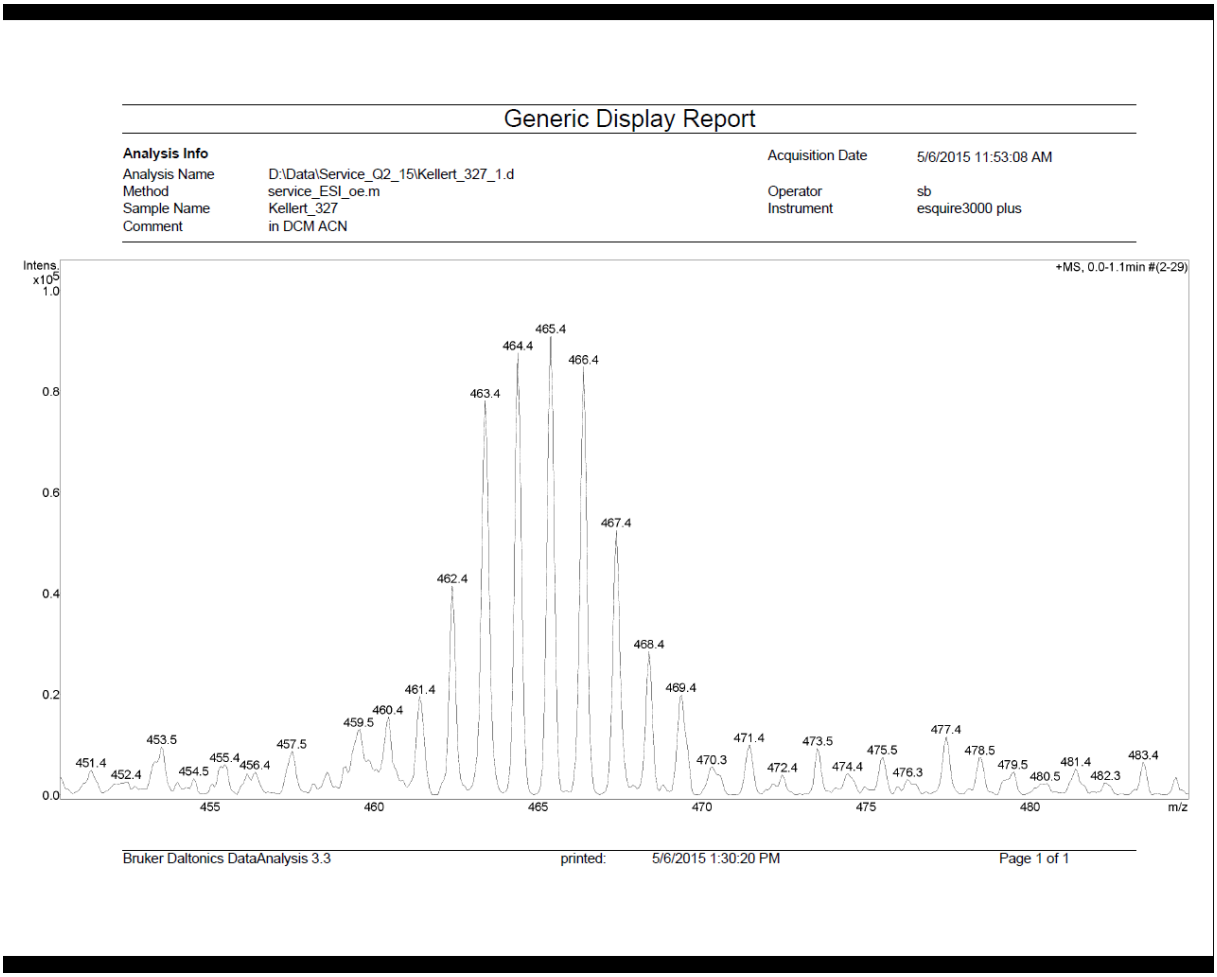


Figure S18: Section of the ESI MS of compound **3**.

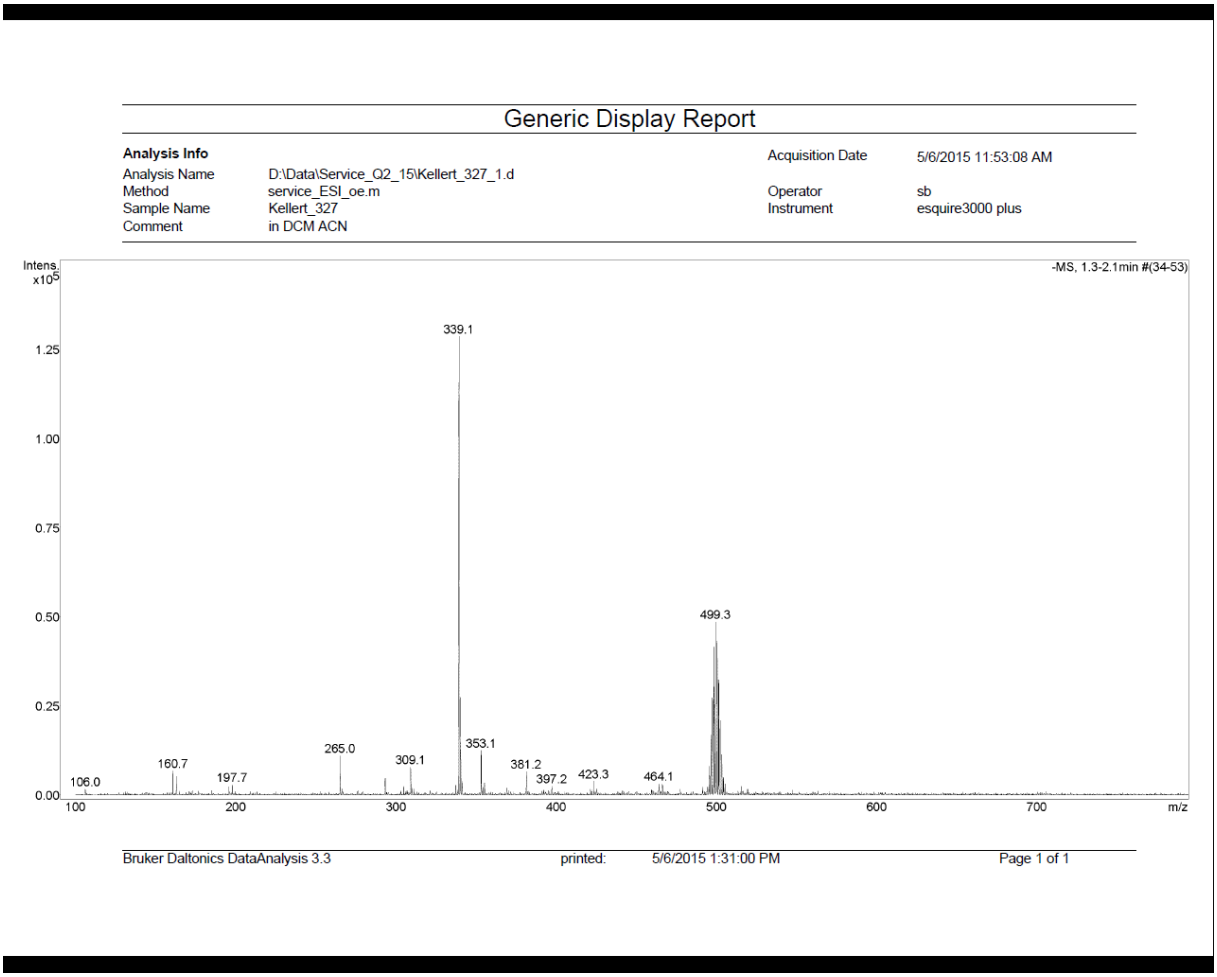


Figure S19: ESI MS (negative mode) of compound **3**.

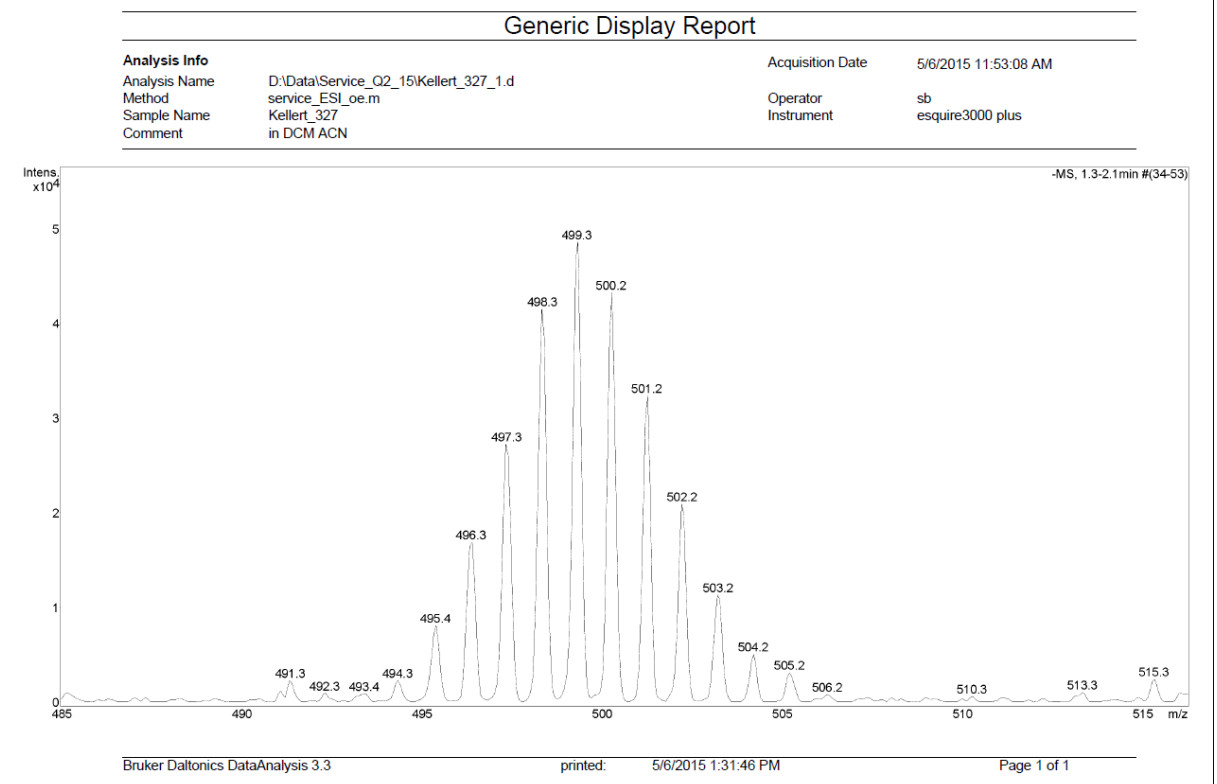
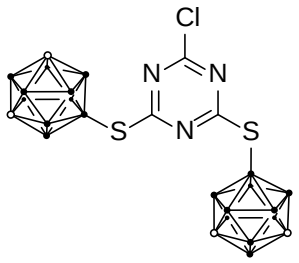


Figure S20: Section of the ESI MS of compound **3**.



3

Empirical formula	$C_7H_{22}B_{20}Cl_1N_3S_2$
Formula weight	464.04
Temperature	130(2) K
Wavelength	71.073 pm
Crystal system	Monoclinic
Space group	$P2_1/c$

Unit cell dimensions	a = 1352.87(4) pm α = 90°
	b = 1411.68(4) pm β = 98.178(3)°
	c = 1249.64(5) pm γ = 90°
Volume	2.3623(1) nm^3
Z	4
Density (calculated)	1.305 Mg/m^3
Absorption coefficient	0.343 mm^{-1}
F(000)	936
Crystal size	0.5 x 0.04 x 0.04 mm^3
Theta range for data collection	2.19 to 30.75°
Index ranges	–19 ≤ h ≤ 19, –20 ≤ k ≤ 19, –17 ≤ l ≤ 16
Reflections collected	30792
Independent reflections	6750 [R(int) = 0.0598]
Completeness to theta = 28.29°	100.0%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1 and 0.96054
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6750 / 0 / 388
Goodness-of-fit on F^2	1.045
Final R indices [I>2σ(I)]	R_1 = 0.0486, wR_2 = 0.0879
R indices (all data)	R_1 = 0.0800, wR_2 = 0.0975
Residual electron density	0.315 and –0.305 $e \cdot Å^{-3}$

Comments: Structure solution with SHELXS-2013 (direct method). Anisotropic refinement of all non-hydrogen atoms with SHELXL-2018. All H atoms were located on difference Fourier maps calculated at the final stage of the structure refinement. With a displacement parameter and bond length analysis, the carborane carbon atoms C(1), C(2), C(3) and C(4) could clearly be localised.

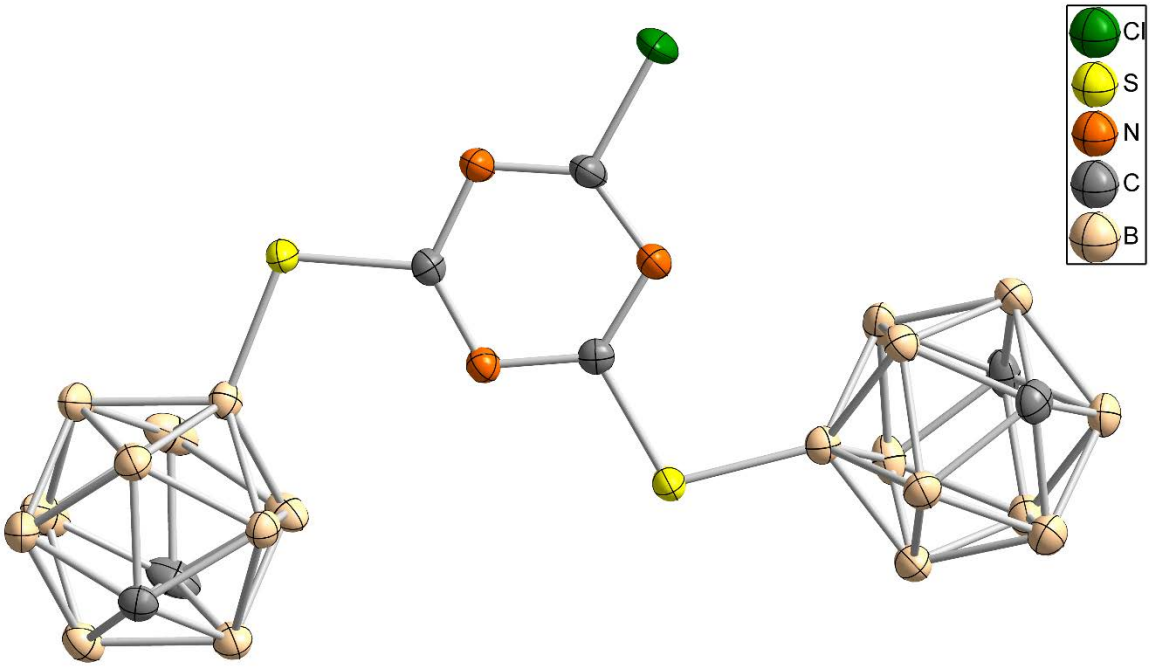


Figure S21: Molecular structure of **3**. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms are omitted for clarity.

5. Additional spectroscopic and crystallographic data of 2-{[4,6-bis(1,7-dicarba-*closo*-dodecaboran-9-ylthio)-1,3,5-triazin-2-yl]thio}acetic acid (4)

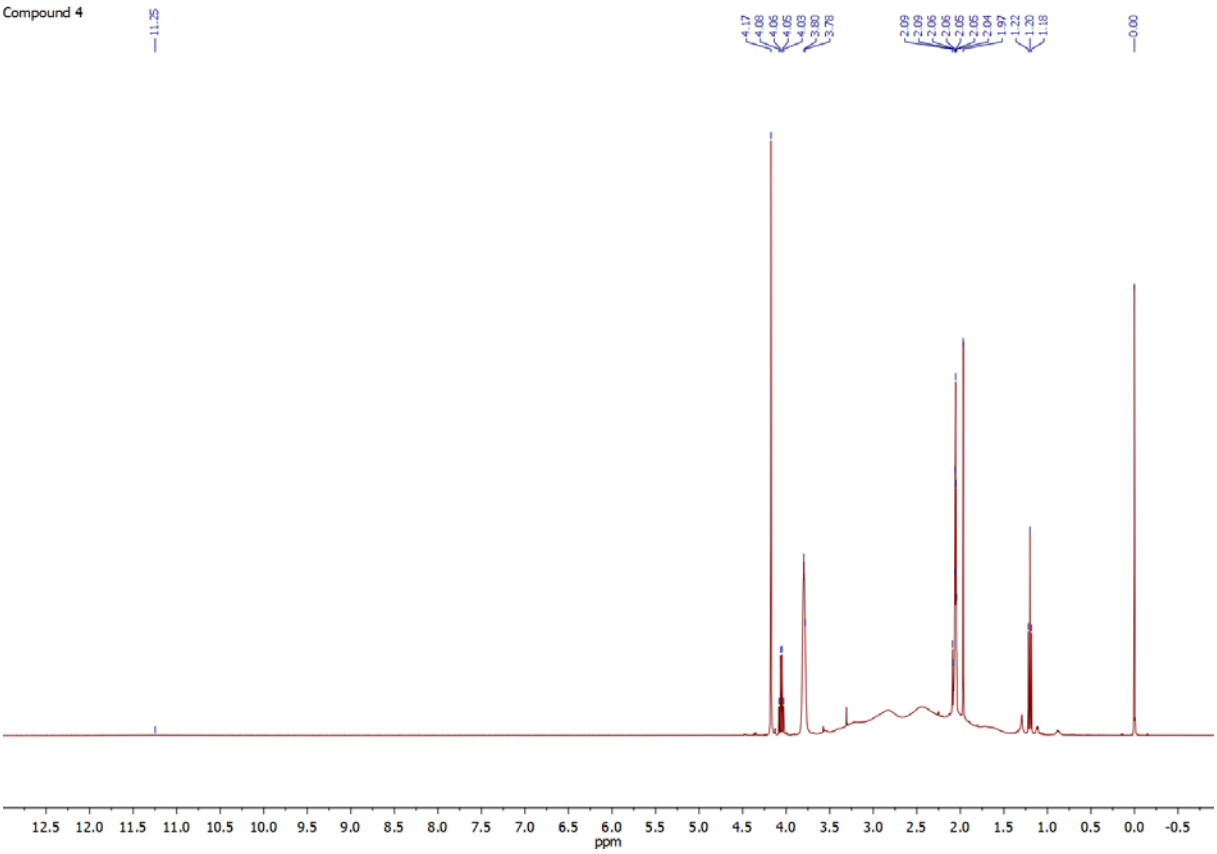


Figure S22: ^{1}H NMR spectrum of compound **4** with ethyl acetate as a minor impurity.

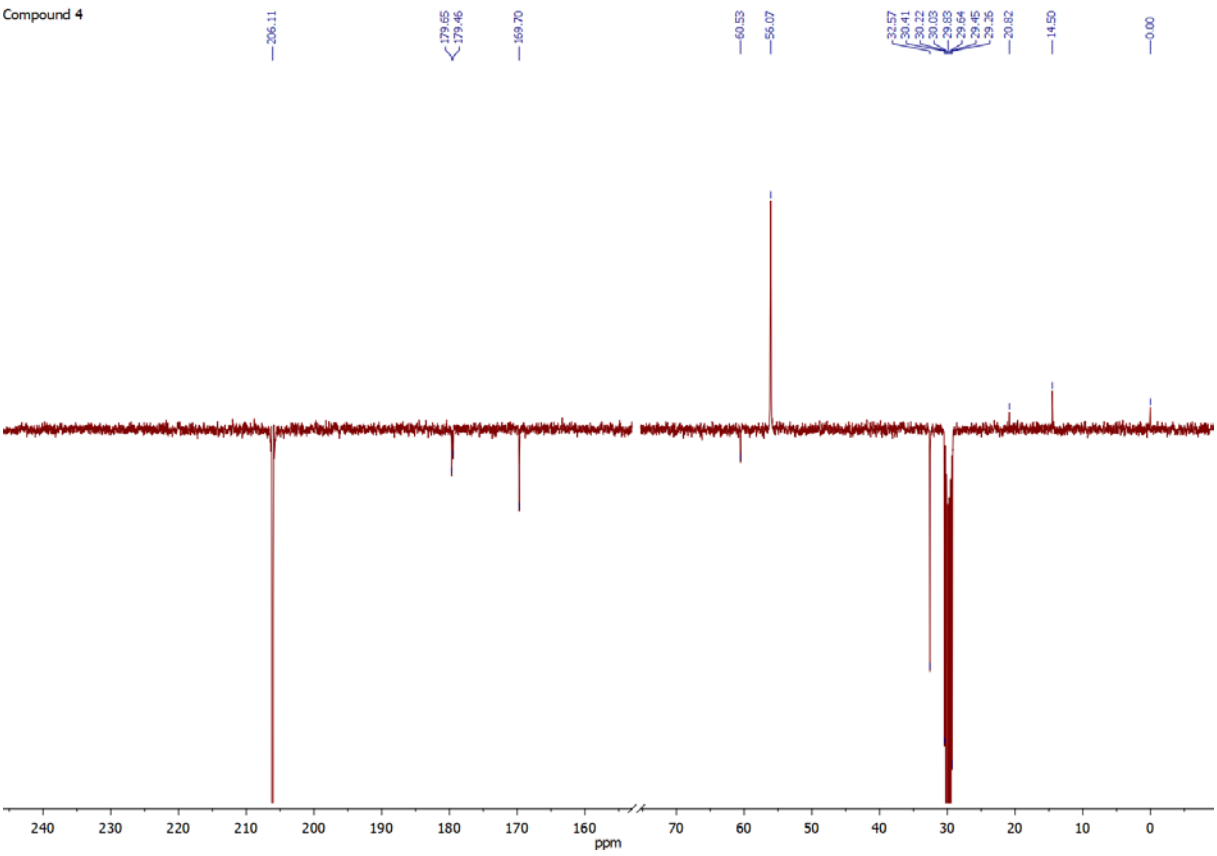


Figure S23: $^{13}C\{^{1}H\}$ NMR spectrum of compound **4** with ethyl acetate as a minor impurity.

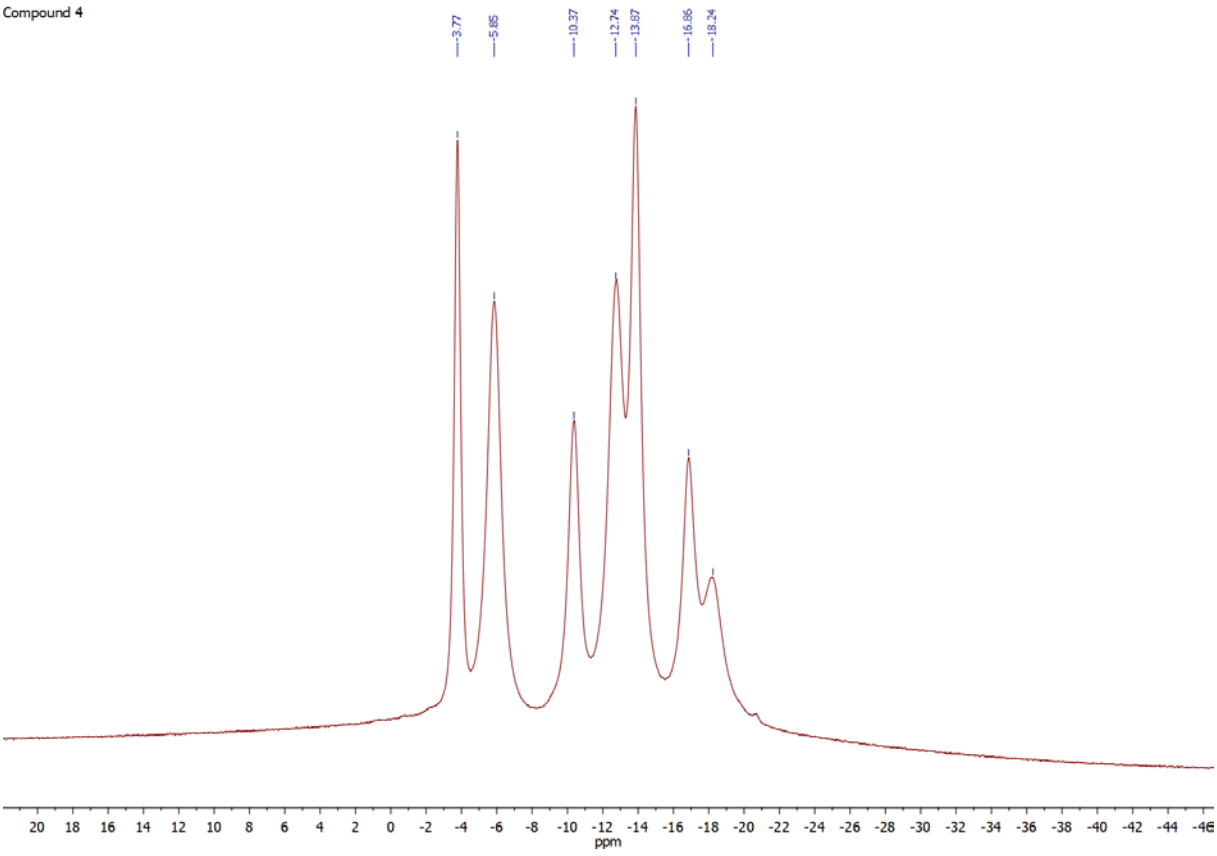


Figure S24: $^{11}B\{^{1}H\}$ NMR spectrum of compound **4**.

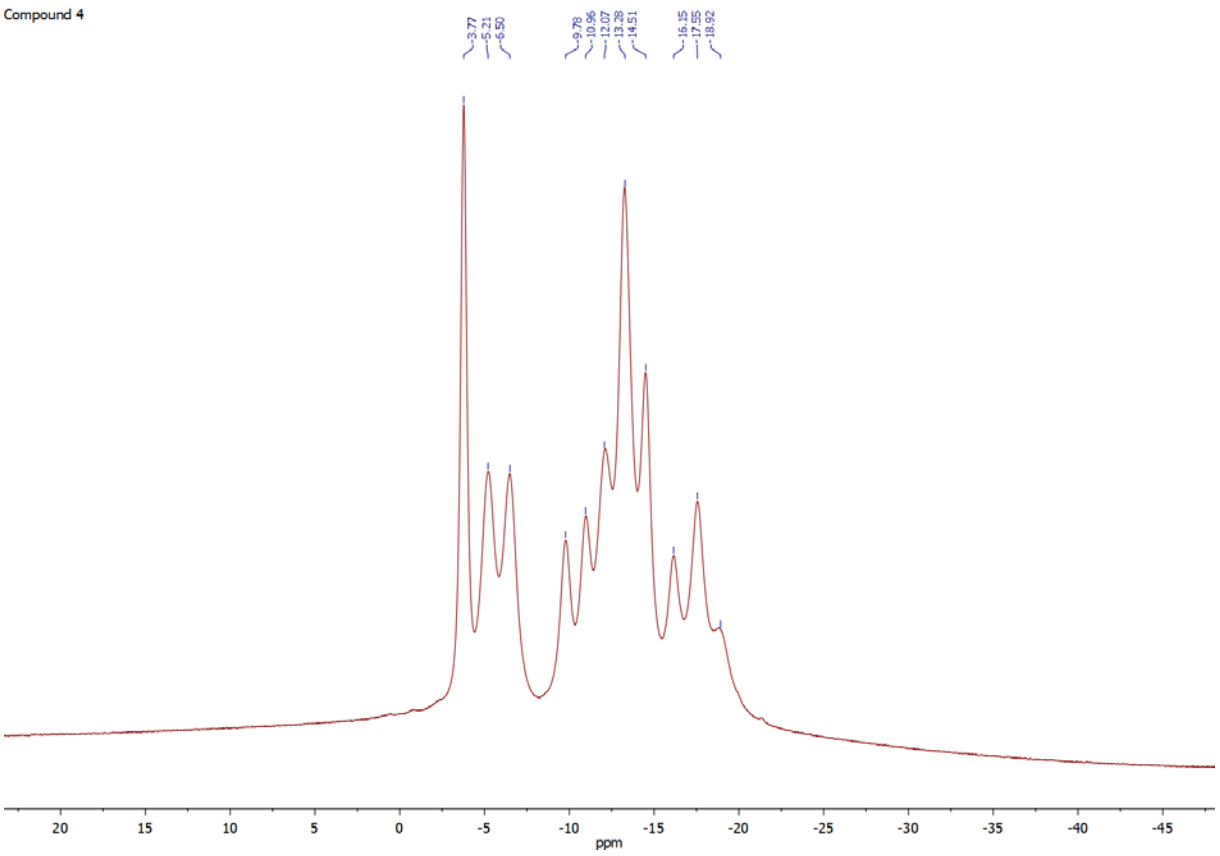


Figure S25: ^{11}B NMR spectrum of compound **4**.

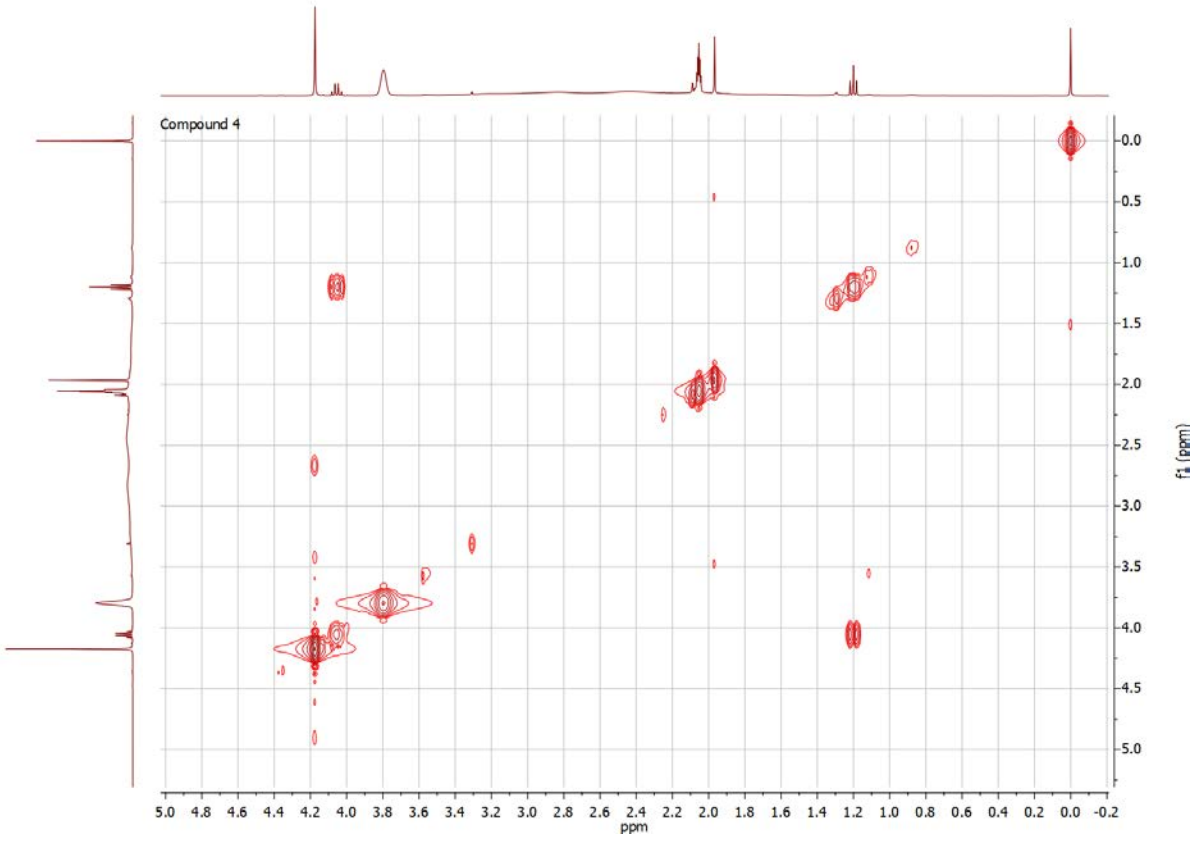


Figure S26: ^{1}H-^{1}H-COSY NMR spectrum of compound **4**.

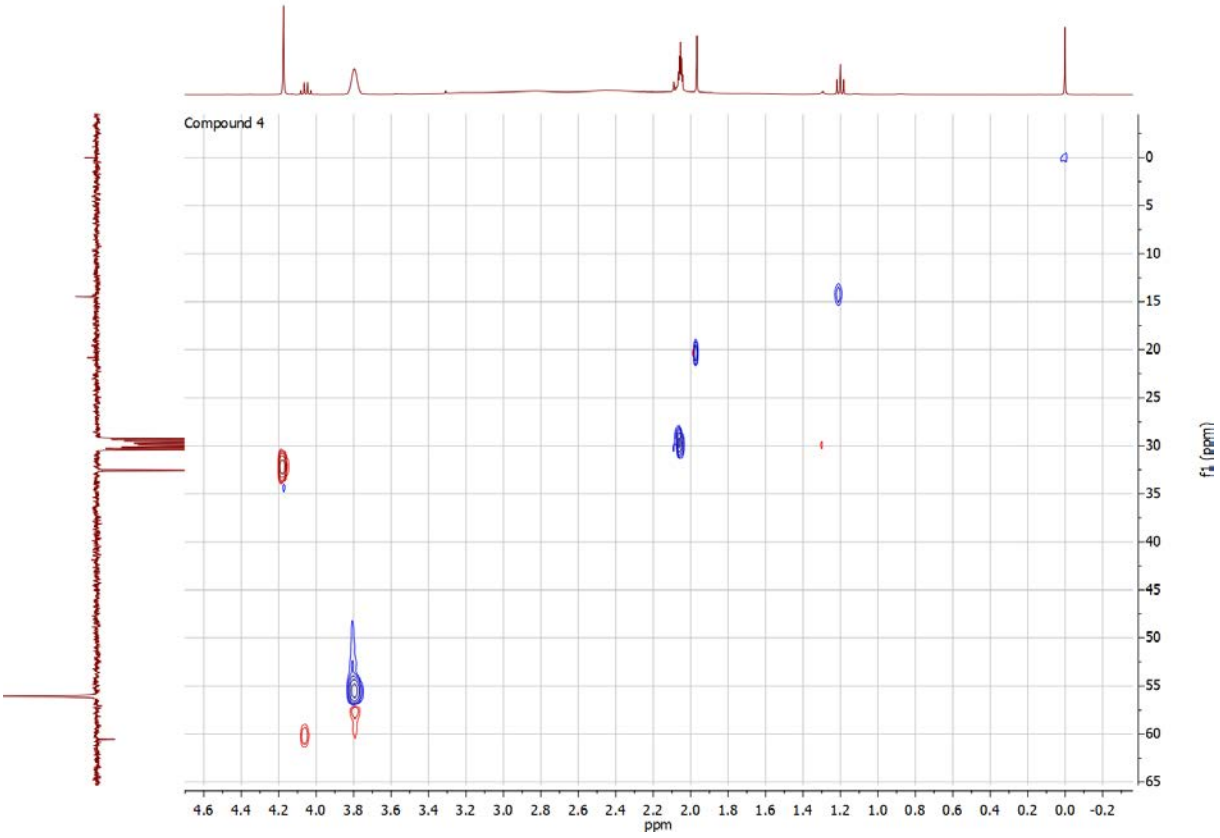


Figure S27: ^{1}H-^{13}C-HSQC NMR spectrum of compound **4**.

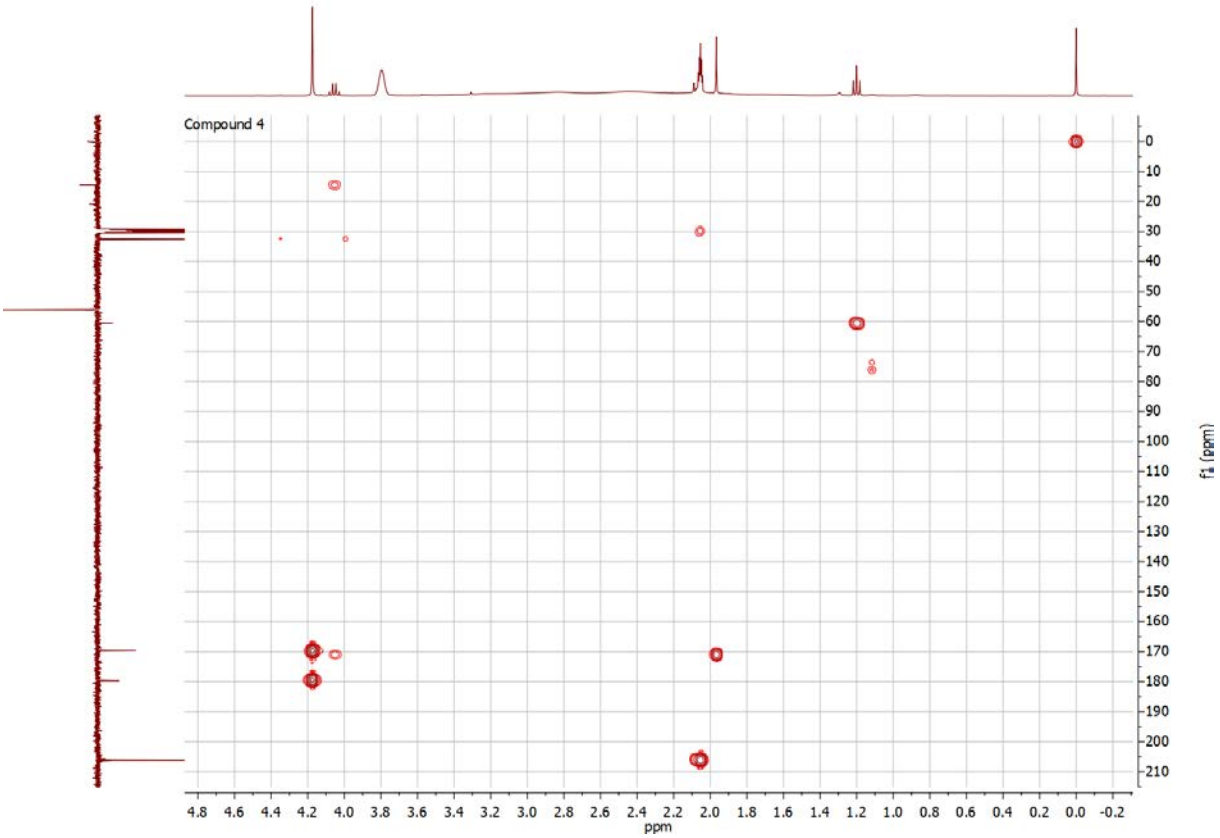


Figure S28: ^{1}H-^{13}C-HMBC NMR spectrum of compound **4**.

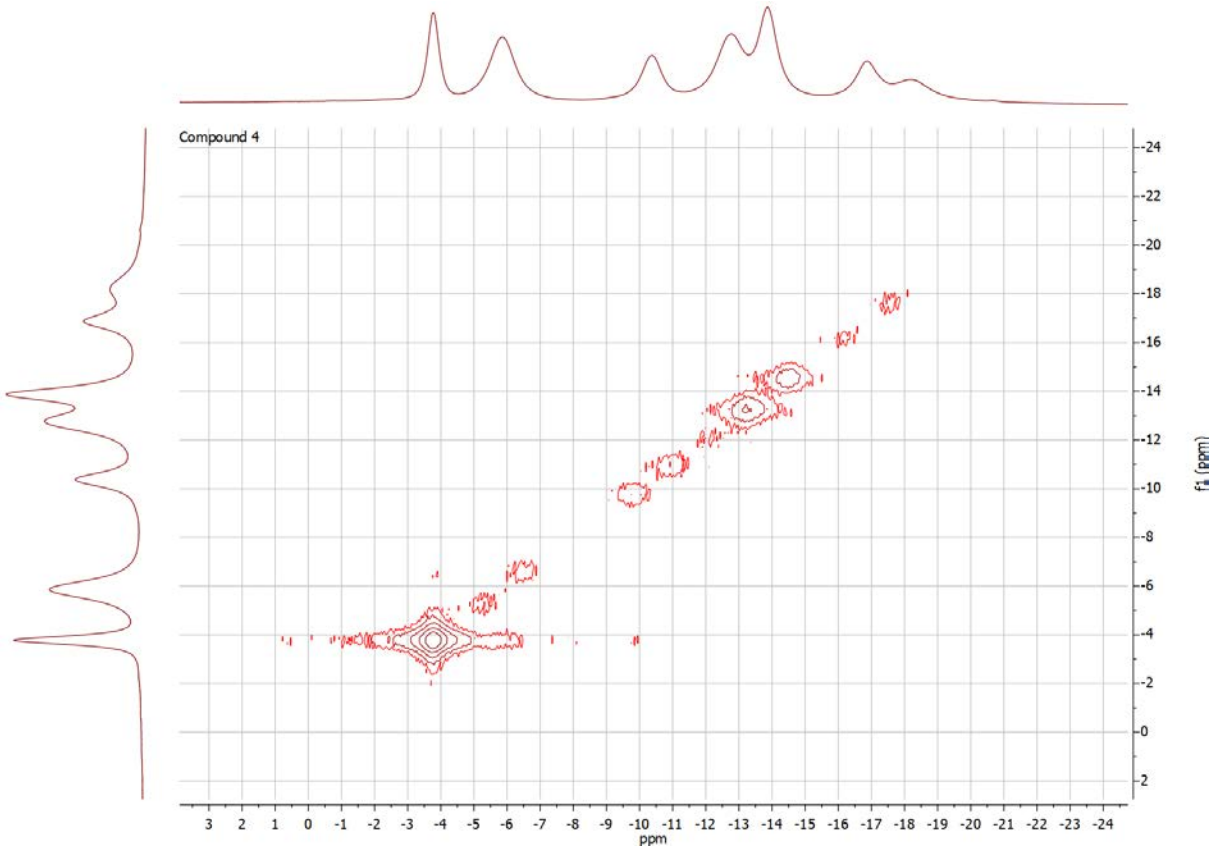


Figure S29: ^{11}B-^{11}B-COSY NMR spectrum of compound **4**.

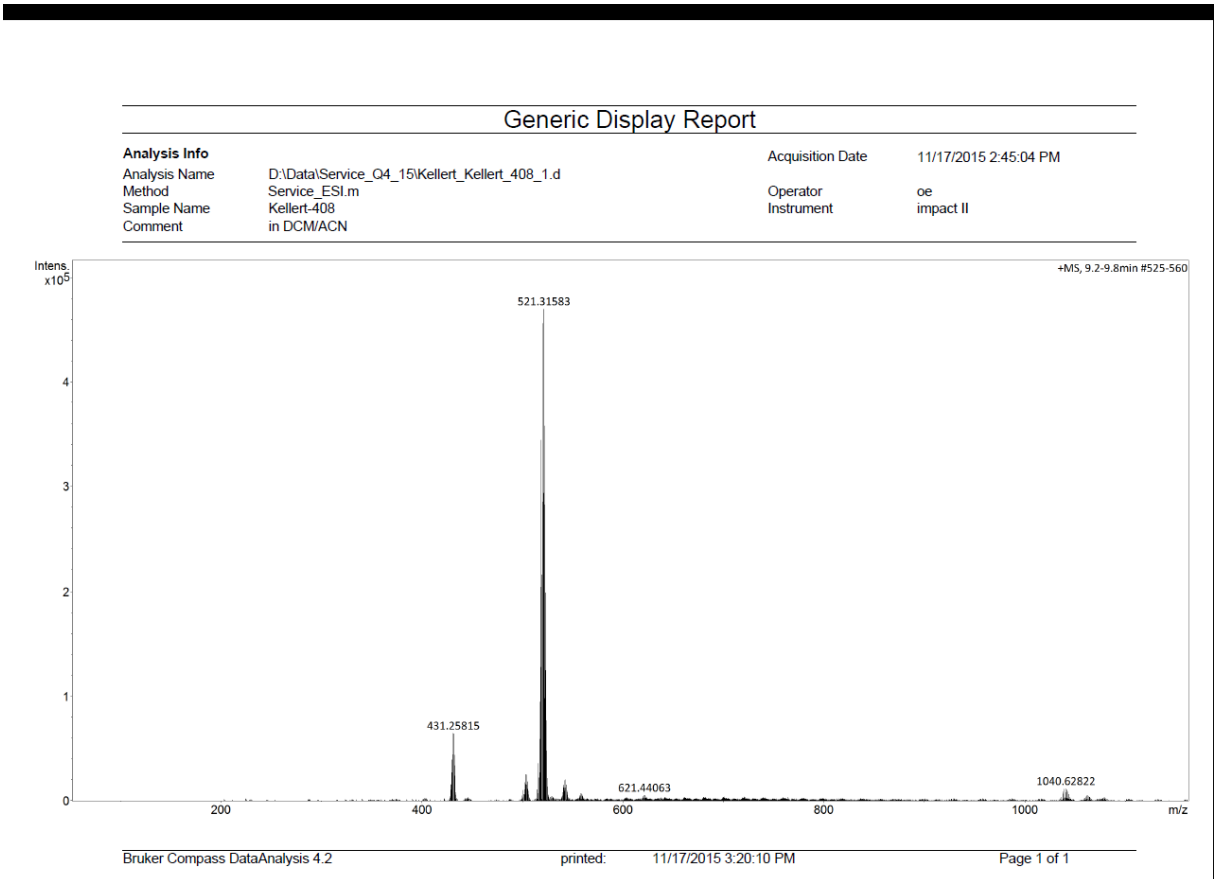


Figure S30: ESI MS (positive mode) of compound **4**.

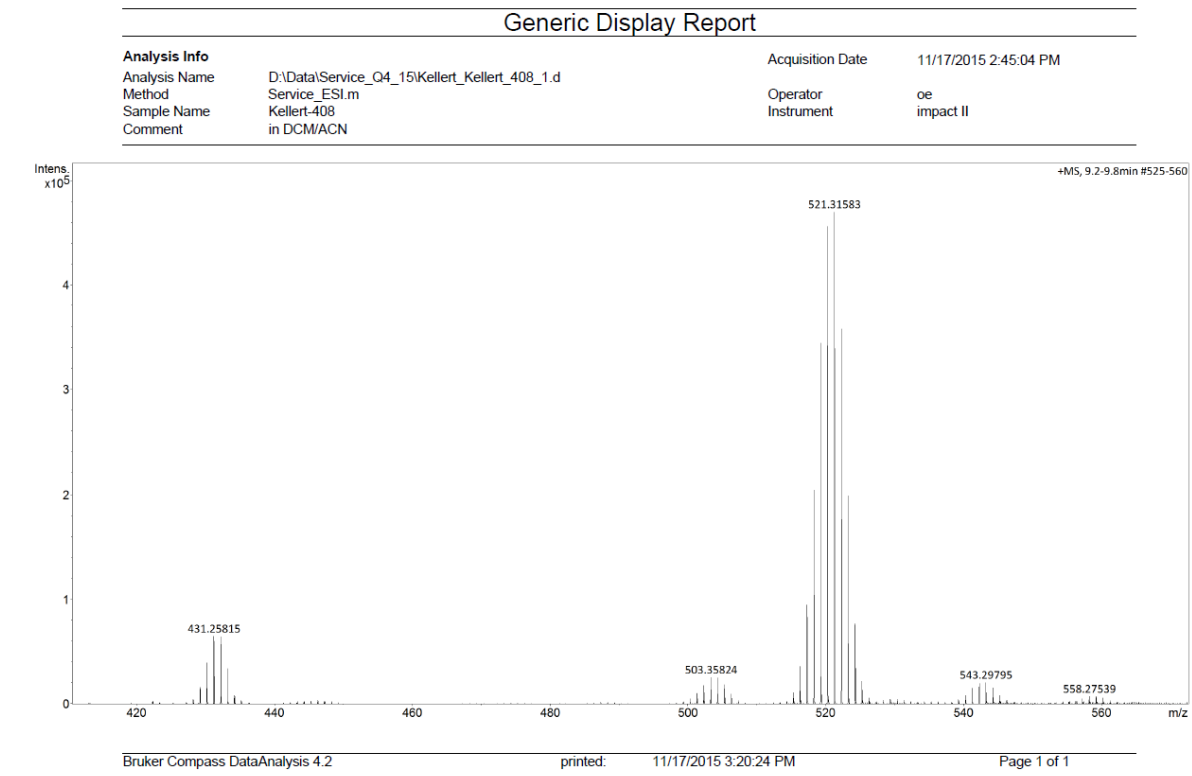


Figure S31: Section of the ESI MS of compound **4**.

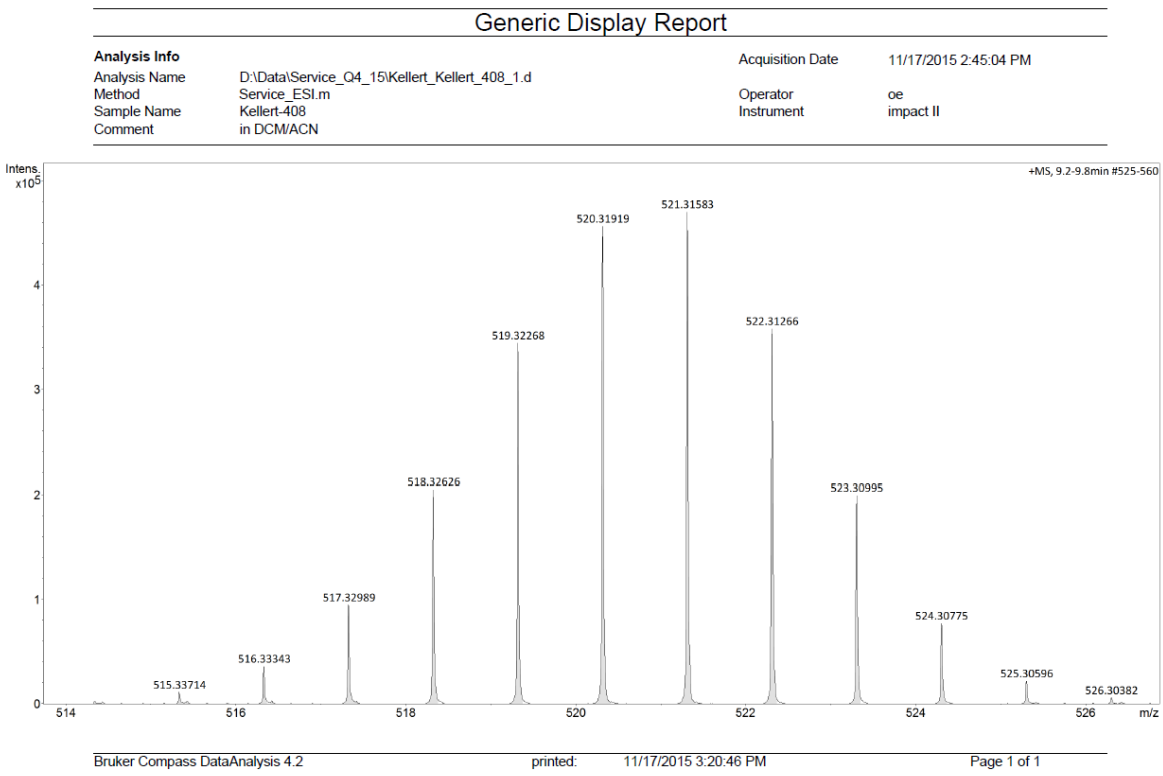
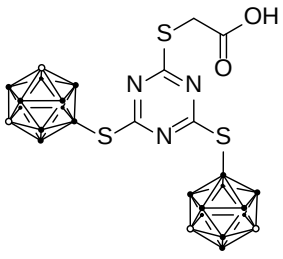


Figure S32: Section of the ESI MS of compound **4**.



4

Empirical formula	$C_{11}H_{32.35}B_{20}N_3O_{3.68}S_3$
Formula weight	577.97
Temperature	130(2) K
Wavelength	71.073 pm
Crystal system	Monoclinic
Space group	$P2_1/n$

Unit cell dimensions	a = 714.00(3) pm α = 90°
	b = 2078.27(6) pm β = 96.755(3)°
	c = 2031.19(5) pm γ = 90°
Volume	2.9931(2) nm^3
Z	4
Density (calculated)	1.283 Mg/m^3
Absorption coefficient	0.274 mm^{-1}
F(000)	1187
Crystal size	0.65 x 0.09 x 0.07 mm^3
Theta range for data collection	2.019 to 32.404°
Index ranges	–10 ≤ h ≤ 10, –31 ≤ k ≤ 13, –29 ≤ l ≤ 29
Reflections collected	19558
Independent reflections	9754 [R(int) = 0.0287]
Completeness to theta = 30.510°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.90570
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9754 / 3 / 463
Goodness-of-fit on F^2	1.032
Final R indices [I>2σ(I)]	R_1 = 0.0637, wR_2 = 0.1613
R indices (all data)	R_1 = 0.0961, wR_2 = 0.1810
Residual electron density	0.751 and –0.797 e·$Å^{-3}$

Comments: Structure solution with SHELXT-2014 (dual-space method). Anisotropic refinement of all non-hydrogen atoms, except disordered parts of the structure, with SHELXL-2018. Except disordered parts of the structure, all H atoms were located on difference Fourier maps calculated at the final stage of the structure refinement. Disordered molecule: The acid and the methyl ester are co-crystallised in a ratio of 0.678(7):0.322(7). In addition, the acid is crystallised with two methanol molecules whereas the methyl ester is crystallised with one methanol molecule only.

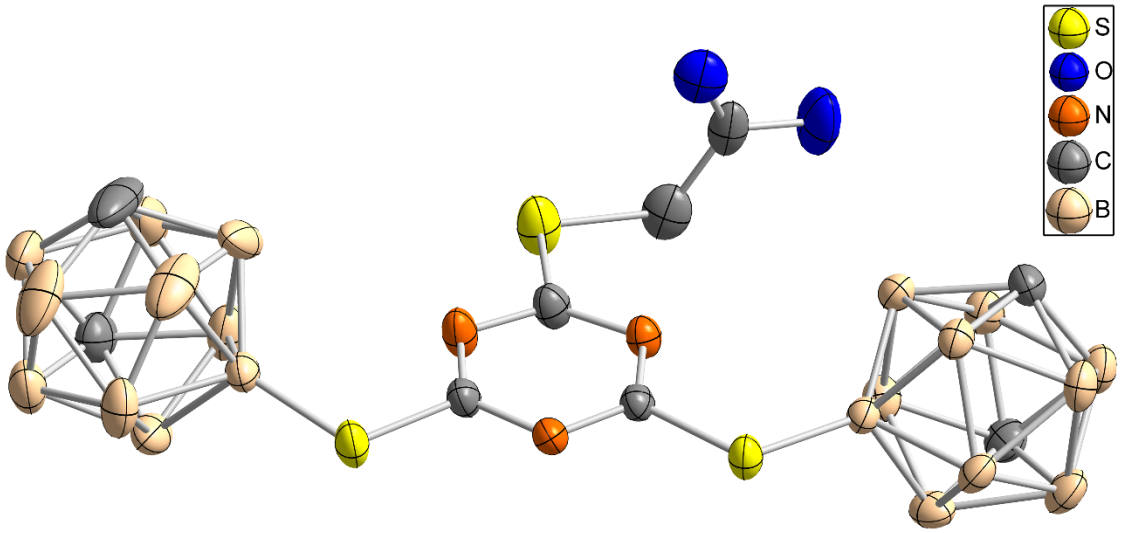


Figure S33: Molecular structure of **4**. Only the carboxylic acid derivative is shown. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms, disorder and solvent molecules are omitted for clarity.

6. Additional spectroscopic and crystallographic data of [4,6-bis(1,7-dicarba-*closo*-dodecaboran-9-ylthio)-1,3,5-triazin-2-yl]glycine (5)

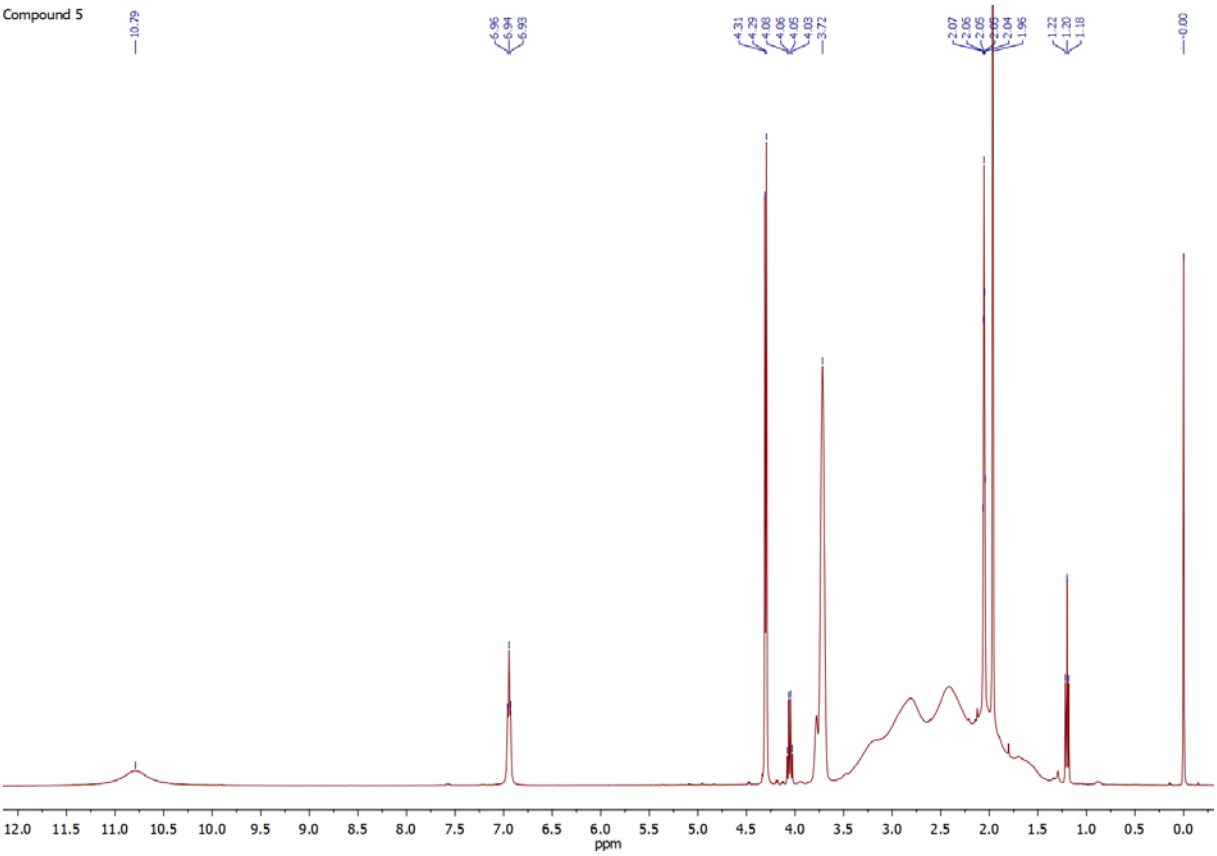


Figure S34: ^{1}H NMR spectrum of compound **5** with ethyl acetate as a minor impurity.

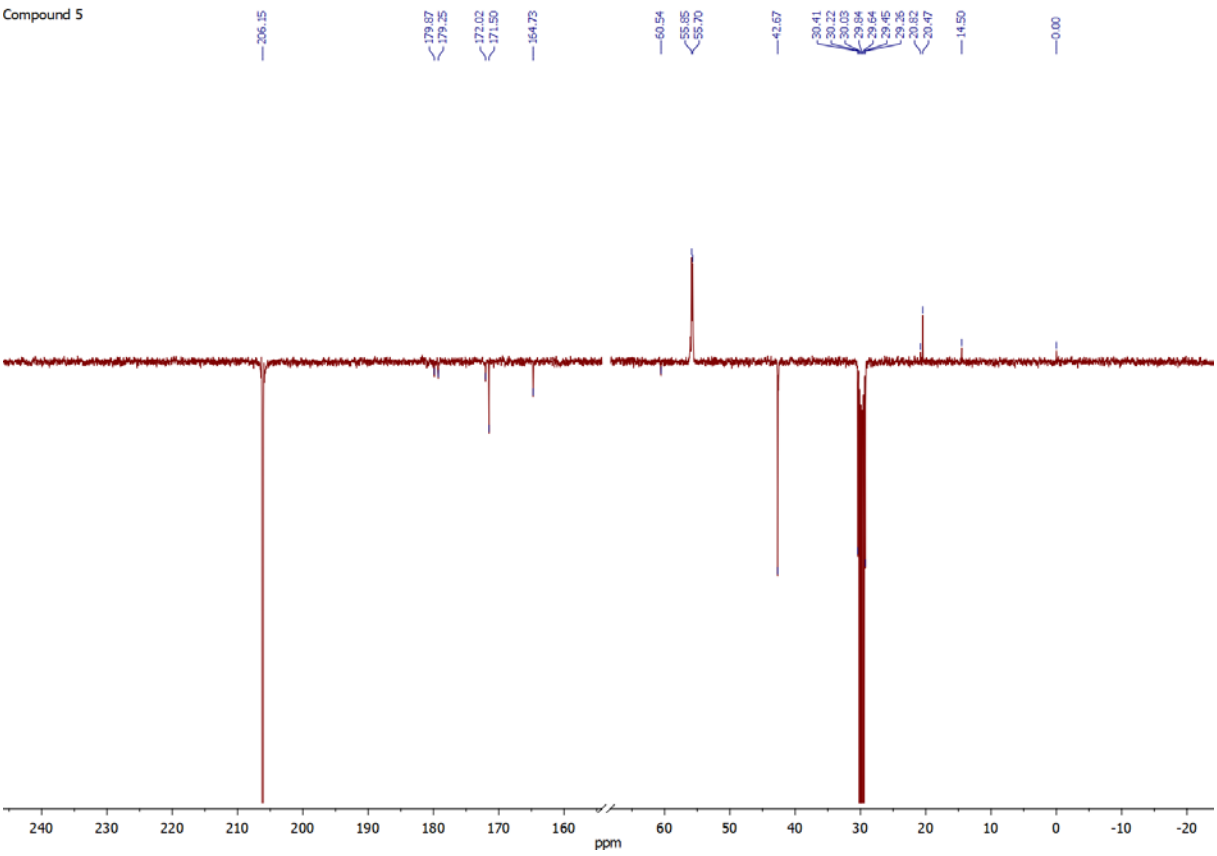


Figure S35: $^{13}C\{^{1}H\}$ NMR spectrum of compound **5** with ethyl acetate as a minor impurity.

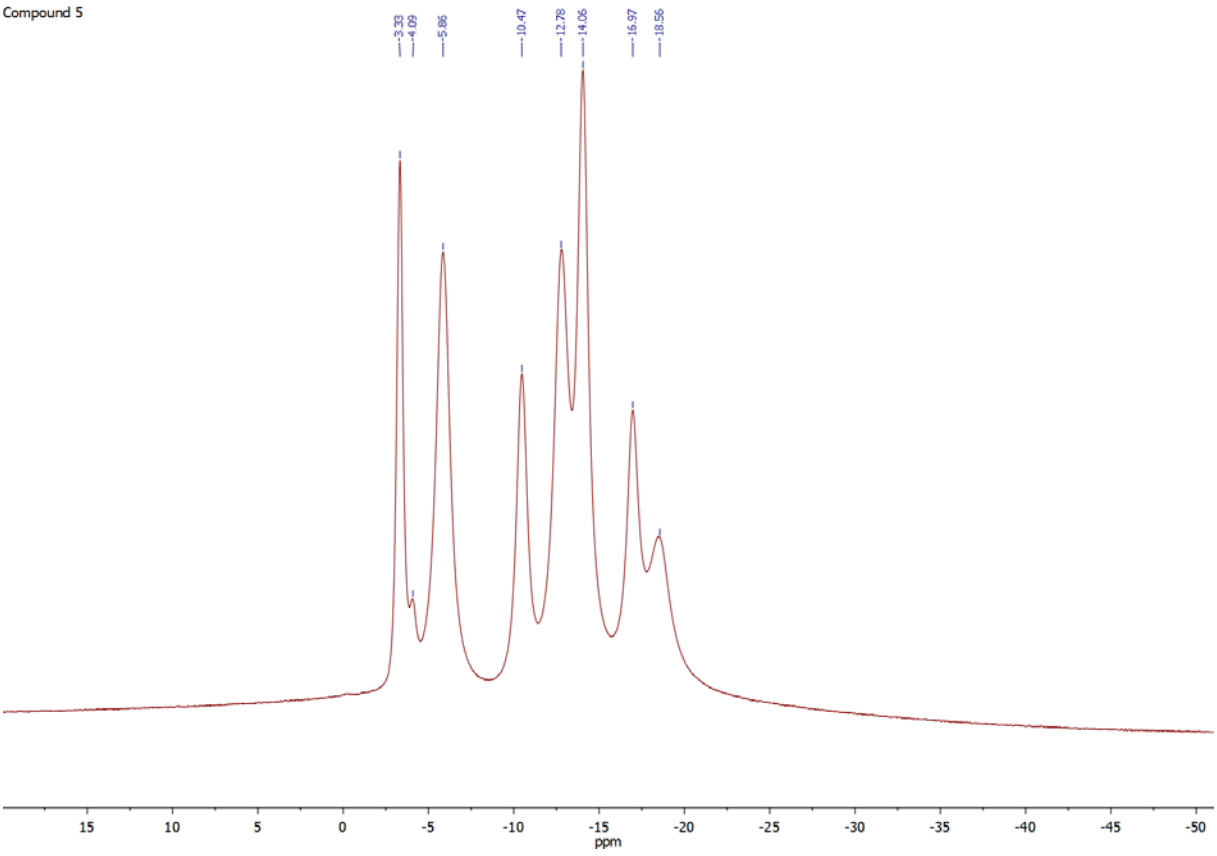


Figure S36: $^{11}B\{^{1}H\}$ NMR spectrum of compound **5**.

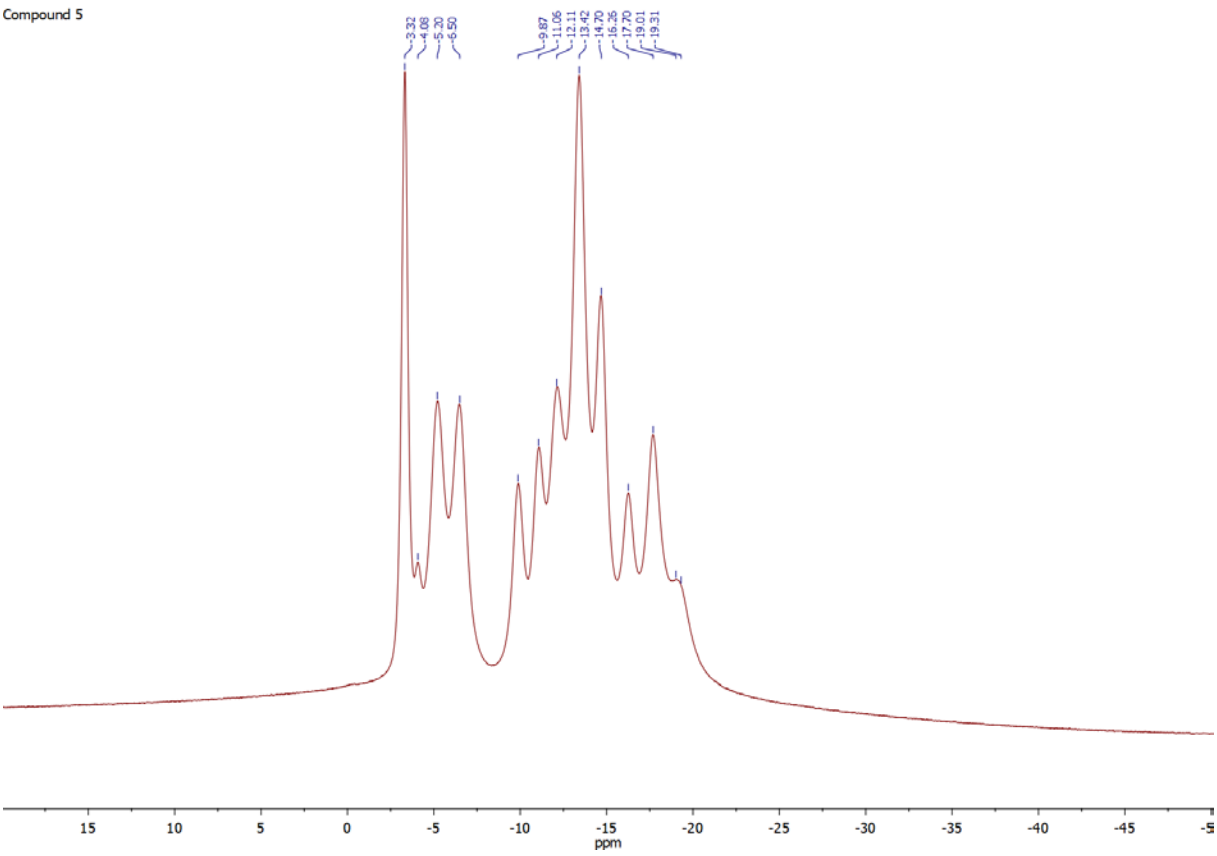


Figure S37: ^{11}B NMR spectrum of compound **5**.

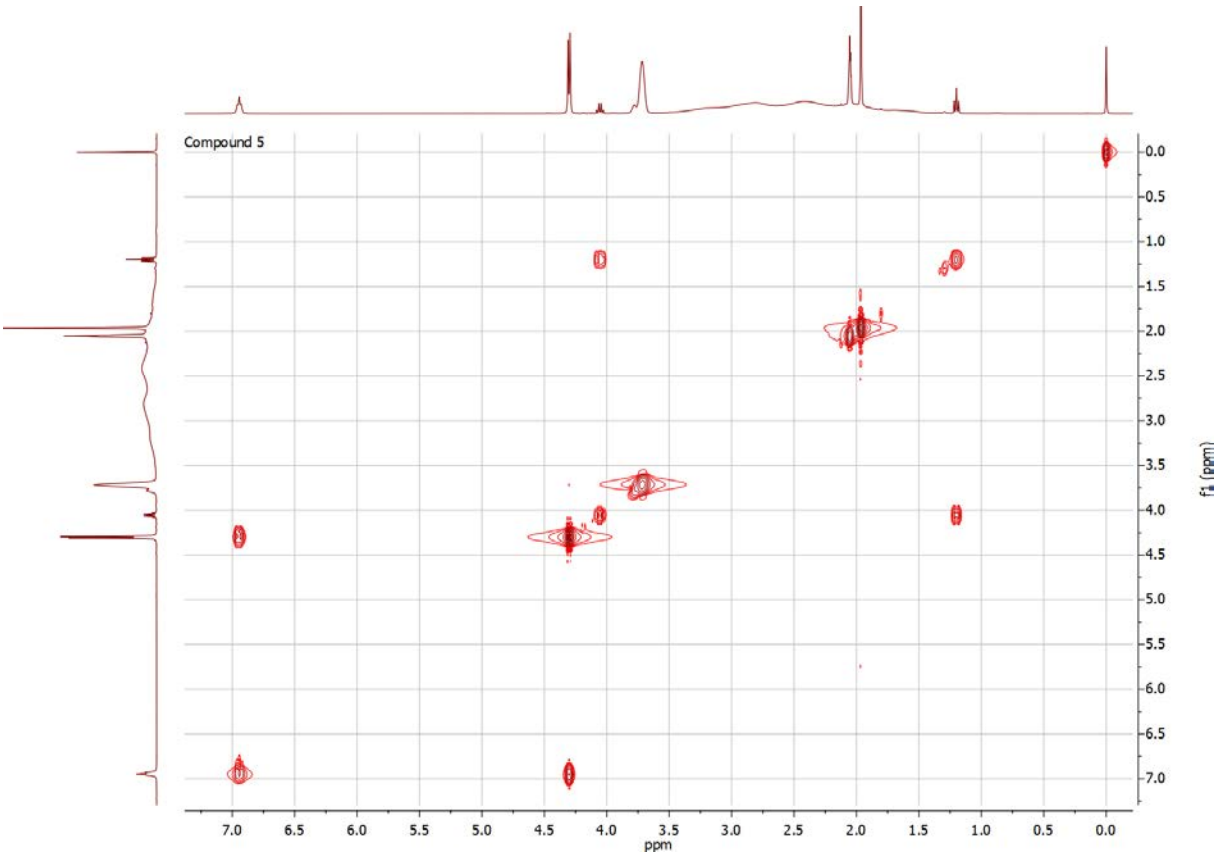


Figure S38: ^{1}H-^{1}H-COSY NMR spectrum of compound **5**.

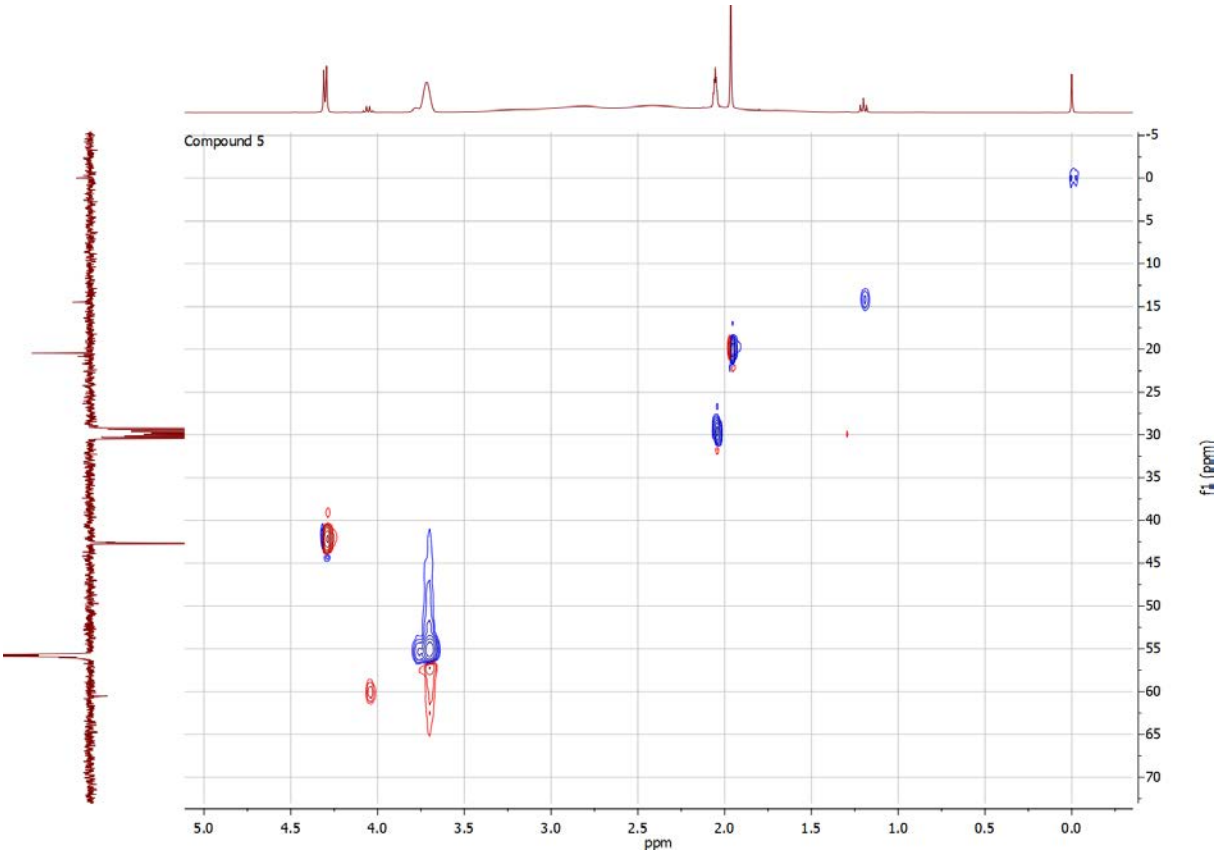


Figure S39: ^{1}H-^{13}C-HSQC NMR spectrum of compound **5**.

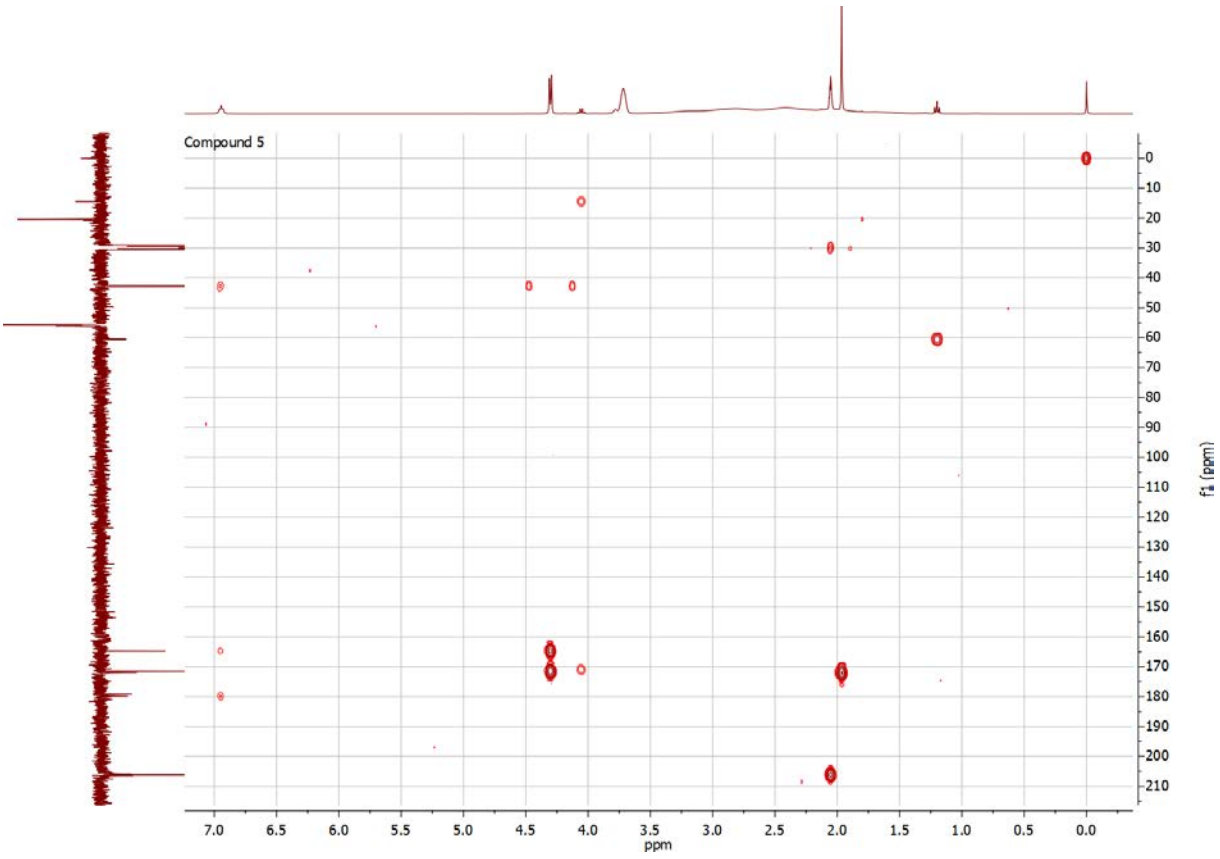


Figure S40: ^{1}H-^{13}C-HMBC NMR spectrum of compound **5**.

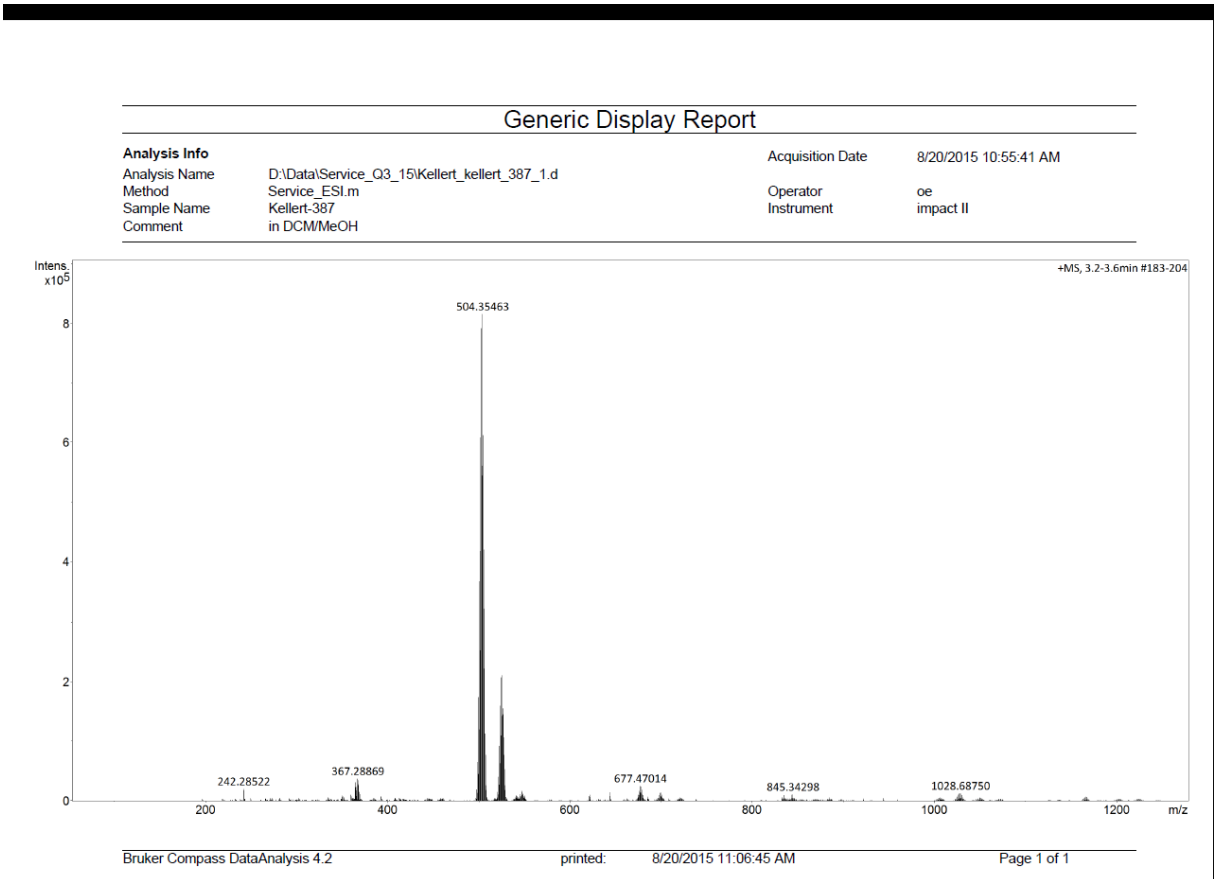


Figure S41: ESI MS (positive mode) of compound **5**.

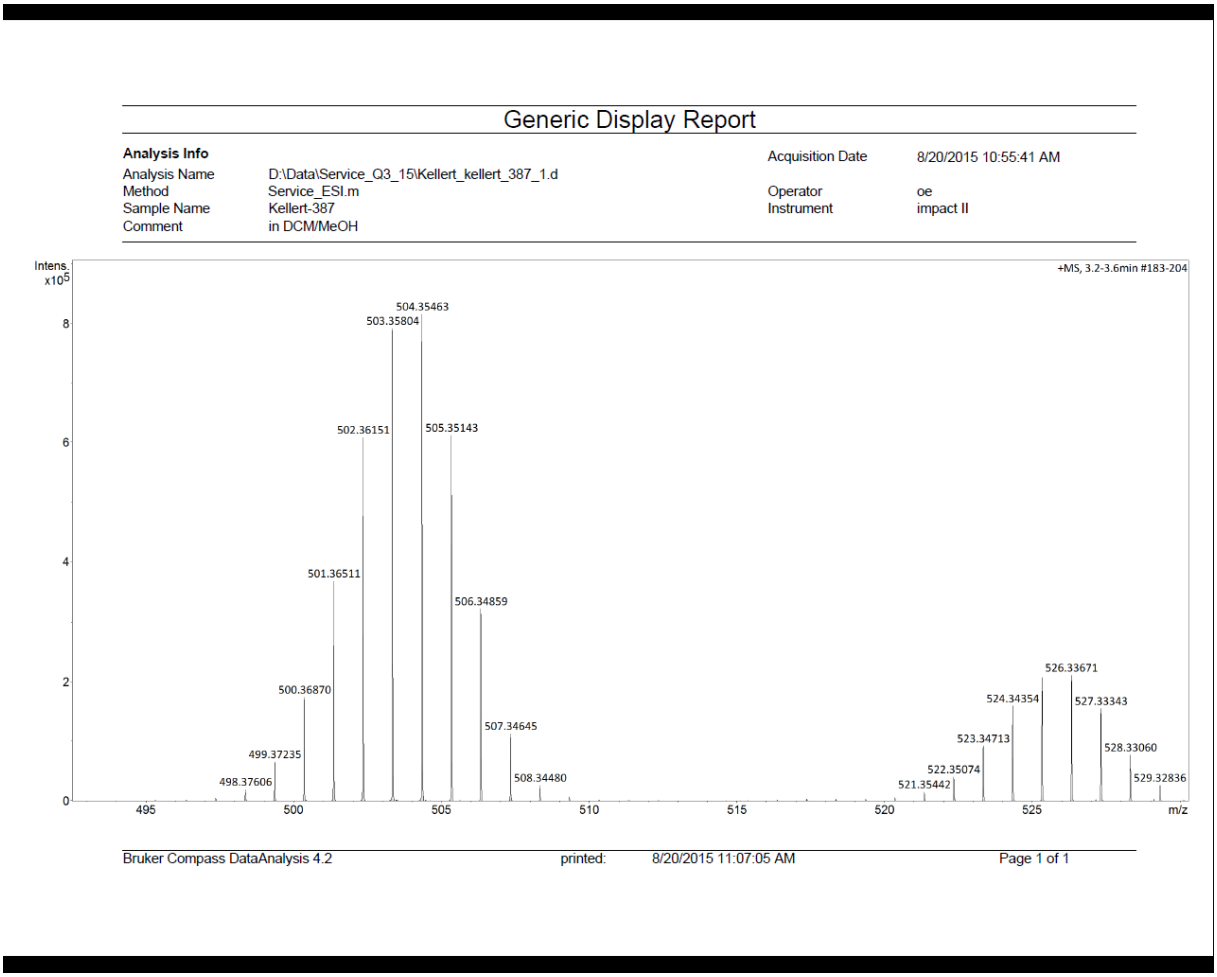


Figure S42: Section of the ESI MS of compound **5**.

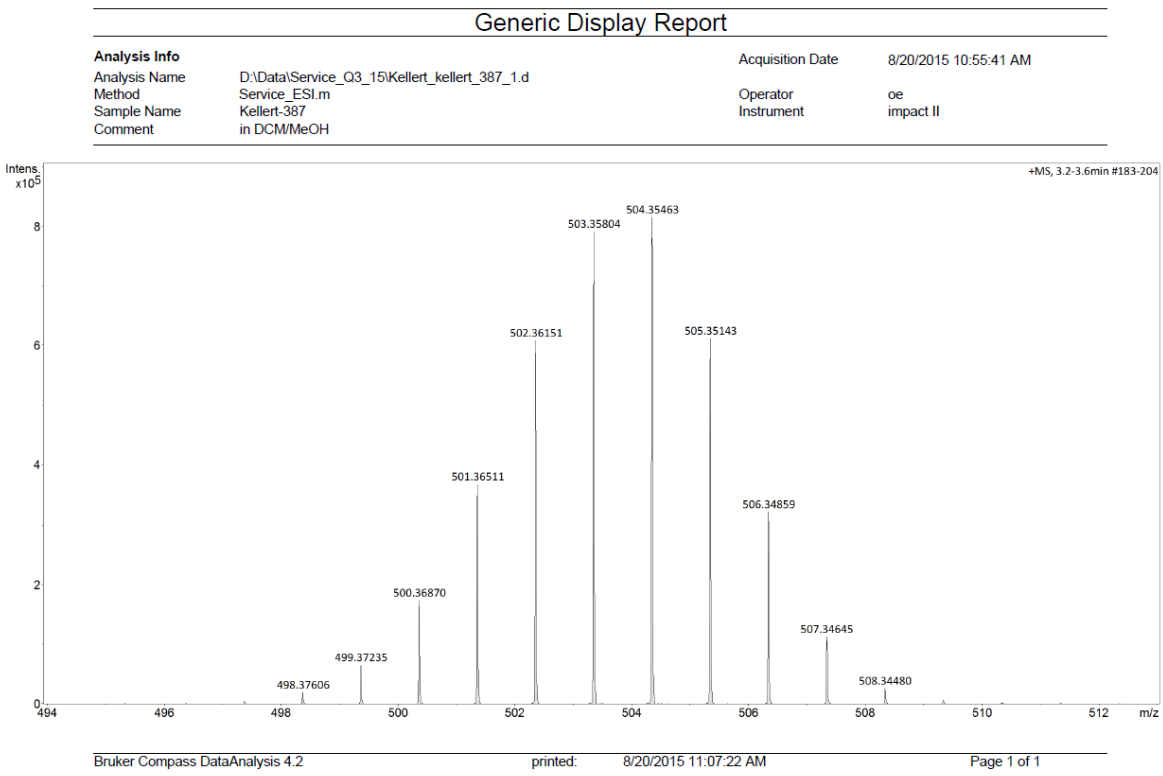
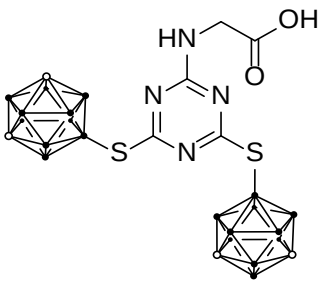


Figure S43: Section of the ESI MS of compound **5**.



5

Empirical formula	$C_{36}H_{90}B_{60}Cl_{18}N_{12}O_7S_6$
Formula weight	2282.25
Temperature	130(2) K
Wavelength	71.073 pm
Crystal system	Monoclinic
Space group	*Cc*
Unit cell dimensions	a = 2061.73(7) pm α = 90°

	b = 4052.0(1) pm β = 99.327(3)°
	c = 1310.75(3) pm γ = 90°
Volume	10.8054(5) nm^3
Z	4
Density (calculated)	1.403 Mg/m^3
Absorption coefficient	0.619 mm^{-1}
F(000)	4592
Crystal size	0.4 x 0.3 x 0.2 mm^3
Theta range for data collection	1.80 to 30.35°
Index ranges	–28 ≤ h ≤ 29, –57 ≤ k ≤ 57, –18 ≤ l ≤ 18
Reflections collected	78082
Independent reflections	28908 [R(int) = 0.0416]
Completeness to theta = 28.29°	100.0%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1 and 0.917
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	28908 / 623 / 1312
Goodness-of-fit on F^2	1.024
Final R indices [I>2σ(I)]	R_1 = 0.0800, wR_2 = 0.2086
R indices (all data)	R_1 = 0.1082, wR_2 = 0.2332
Racemic twin	
Twin domain ratio	0.58(8):0.42(8)
Residual electron density	0.812 and –1.103 e·$Å^{-3}$

Comments: Structure solution with SHELXT-2014 (dual space method). Anisotropic refinement of all non-hydrogen atoms, except disordered parts of the structure, with SHELXL-2018. All hydrogen atoms are calculated on idealised positions. All solvent molecules (chloroform and acetone) are disordered. For an acceptable interpretation of the electron density map, some of the highly disordered chloroform molecules are treated as three- or fourfold disordered. Most likely as a result of the loosely packed solvent molecules, one carborane unit (C(26), C(27), B(51) to B(60)) is found to be disordered as well with a ratio of 0.61(1):0.39(1). The carbon atoms of the carborane units could not be localised. The molecular formula of the compound can be given as $(C_9H_{26}B_{20}N_4O_2S_2)_3 \cdot 6\ CHCl_3 \cdot 1$ acetone. Significant intermolecular OH···N and NH···O hydrogen donor-acceptor bonds are present forming a trimer (shown in Figures S45 and Table S1).

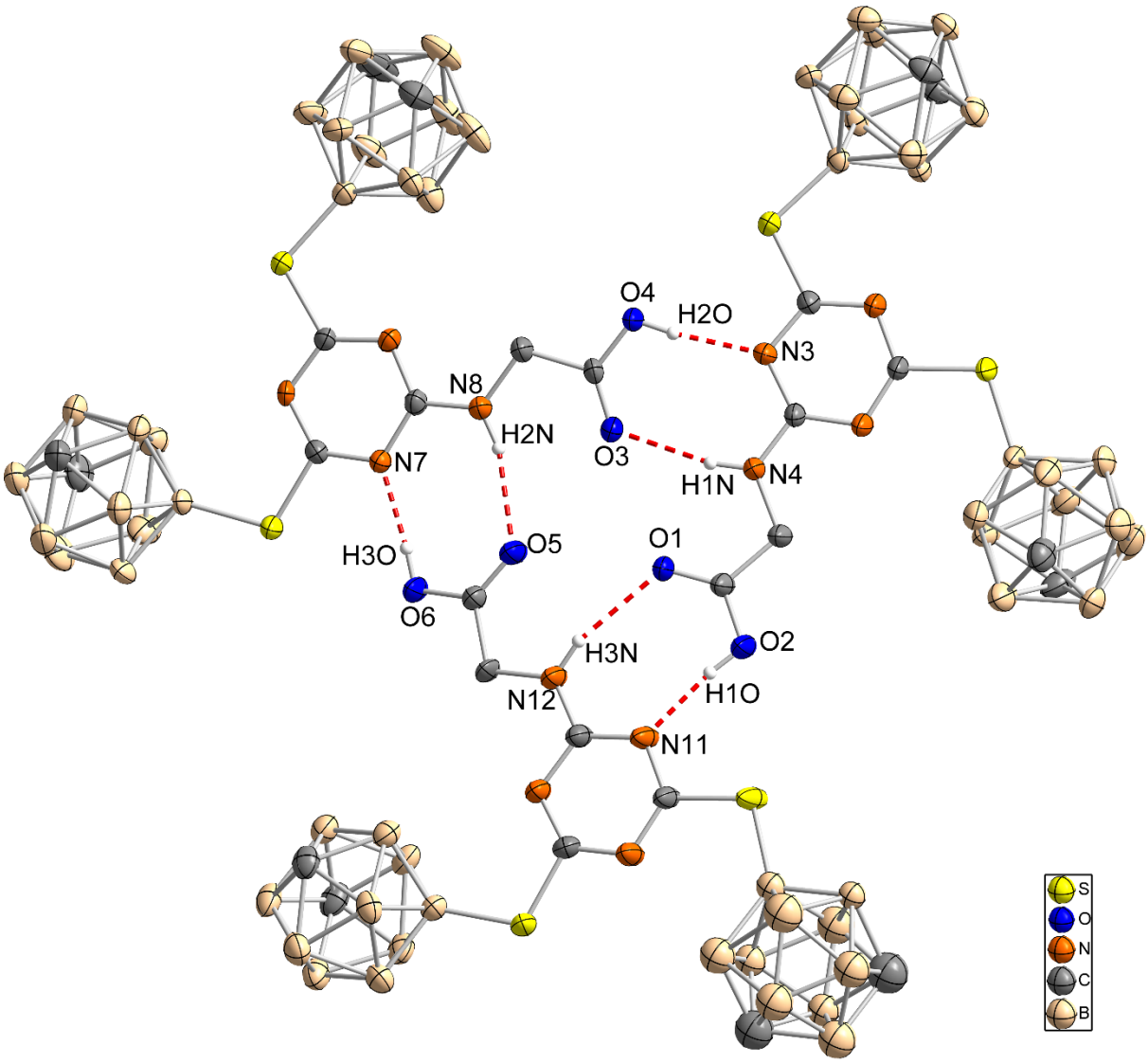


Figure S44: Molecular structure of **5**. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms are drawn with a fixed atom radius of 13.5 pm. Solvent molecules and hydrogen atoms, which are not involved in hydrogen bonding, are omitted for clarity.

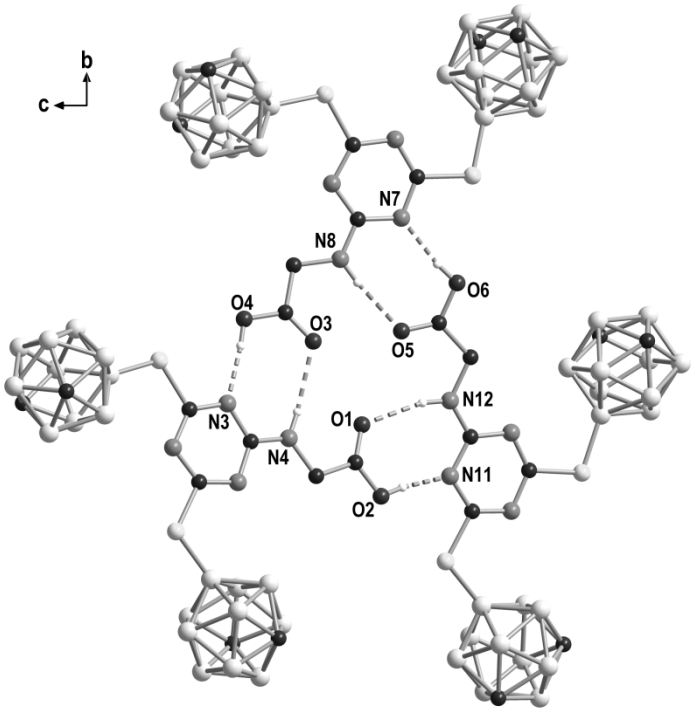


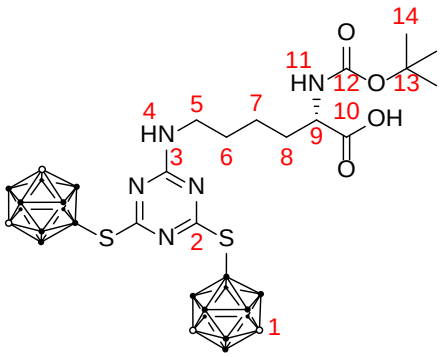
Figure S45: Intermolecular OH···N and NH···O donor-acceptor bonds in the molecular structure of **5** (viewed along the *a* axis). Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms are drawn with a fixed atom radius of 13.5 pm. Hydrogen atoms, which are not involved in hydrogen bonding, are omitted for clarity

Table S1: Hydrogen bonds for **5** [pm and °].

D-H···A	d(D–H)	d(H···A)	d(D···A)	<(DHA)
O(2)–H(1O)···N(11)	84	184	267.3(8)	171.9
O(4)–H(2O)···N(3)	84	187	270.6(6)	173.5
O(6)–H(3O)···N(7)	84	184	266.8(6)	170.6
N(4)–H(1N)···O(3)	88	219	303.5(6)	161.1
N(8)–H(2N)···O(5)	88	219	302.1(6)	157.6
N(12)–H(3N)···O(1)	88	221	306.0(7)	162.9

Symmetry transformations used to generate equivalent atoms: none; d = bond length or distance; < = bond angle; D = hydrogen bond donor atom; A = hydrogen bond acceptor atom.

7. Assignment of spectroscopic data of N^6-[4,6-bis(1,7-dicarba-*closo*-dodecaboran-9-ylthio)-1,3,5-triazin-2-yl]-N^2-(*tert*-butoxycarbonyl)-L-lysine (6)



6

Assignment of spectroscopic data was based on 2D NMR experiments and selective TOCSY.

^{1}H NMR (400.16 MHz, acetonitrile-d_3): δ = 1.40 (s, 9H, C(C^{14}**H$_3$**)$_3$), 1.50 − 3.30 (br^a, 18H, B$_{10}$**H$_9$**), 1.59 (br, m, 4H, C**H$_2$**, C^{6,7}H$_2$), 1.77 (br, m, 2H, C**H$_2$**, C^{8}H$_2$), 3.38 (br, s, 4H, C$^{1,1'}$**H**), 3.41 (m, 2H, C^5**H$_2$**), 4.04 (m, 1H, C^9**H**), 5.54 (d, $^3J_{HH}$ = 7.8 Hz, 1H, N^{11}**H**), 6.20 (m, 1H, N^4**H**), 9.50 (s, 1H, C^{10}OO**H**) ppm. ^{13}C{^{1}H} NMR (100.63 MHz, acetonitrile-d_3): δ = 23.9 (s, **C**$^{6\text{ or }7}$H$_2$), 28.6 (s, C(**C**^{14}H$_3$)$_3$), 30.2 (s, **C**$^{6\text{ or }7}$H$_2$), 32.1 (s, **C**^{8}H$_2$), 41.2 (s, **C**^{5}H$_2$), 54.4 (s, **C**^{9}H), 55.9 (br, s, 2x**C**$^{1\text{ or }1'}$H), 56.0 (br, s, 2x**C**$^{1\text{ or }1'}$H), 79.9 (s, **C$_q$**^{13}(CH$_3$)$_3$), 156.7 (s, **C$_q$**^{2}S), 174.5 (s, **C$_q$**^{3}), 178.5 (s, **C$_q$**^{12}O), 179.6 (s, **C$_q$**^{10}OOH) ppm. ^{11}B{^{1}H} NMR (128.38 MHz, acetonitrile-d_3): δ = −18.4 (s, 2B), −17.0 (s, 2B), −14.1 (s, 4B), −12.9 (s, 4B), −10.6 (s, 2B), −6.0 (s, 4B), −3.5 (s, 2B, BS) ppm. ^{11}B NMR (128.38 MHz, acetonitrile-d_3): δ = −18.4 (br^a, 2B), −17.0 (br d, $^1J_{BH}$ = 192 Hz, 2B), −13.5 (br^a, 8B), −10.6 (d, $^1J_{BH}$ = 154 Hz, 2B), −6.0 (d, $^1J_{BH}$ = 166 Hz, 4B), −3.5 (s, 2B, BS) ppm.

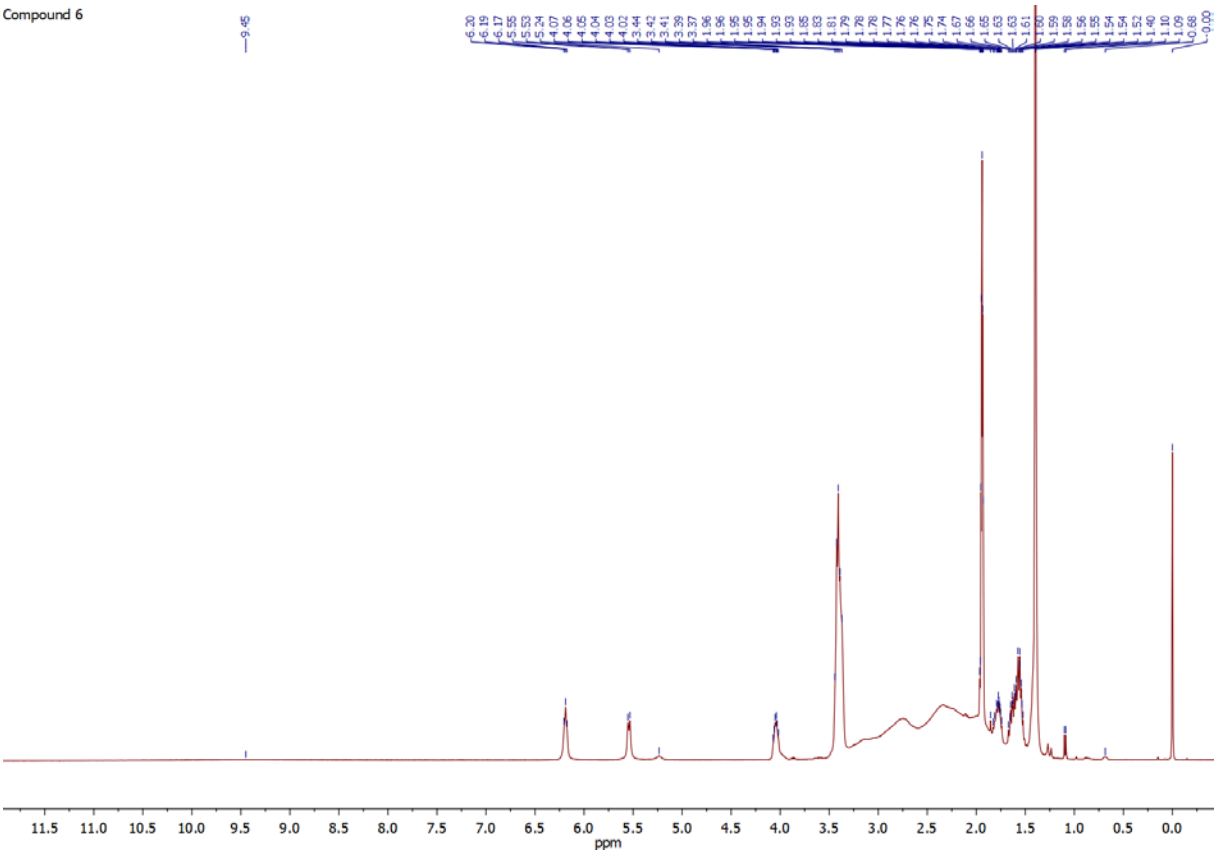


Figure S46: ^{1}H NMR spectrum of compound **6**.

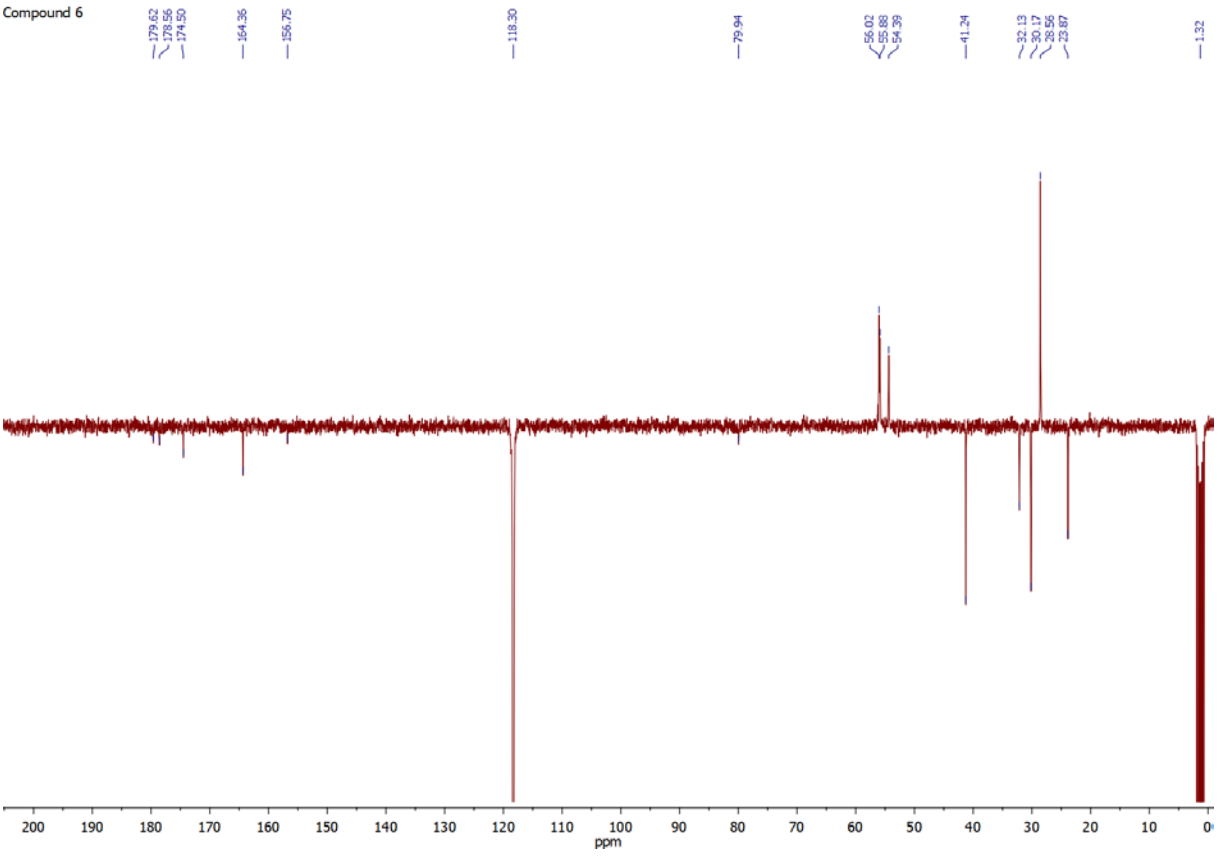


Figure S47: $^{13}C\{^{1}H\}$ NMR spectrum of compound **6**.

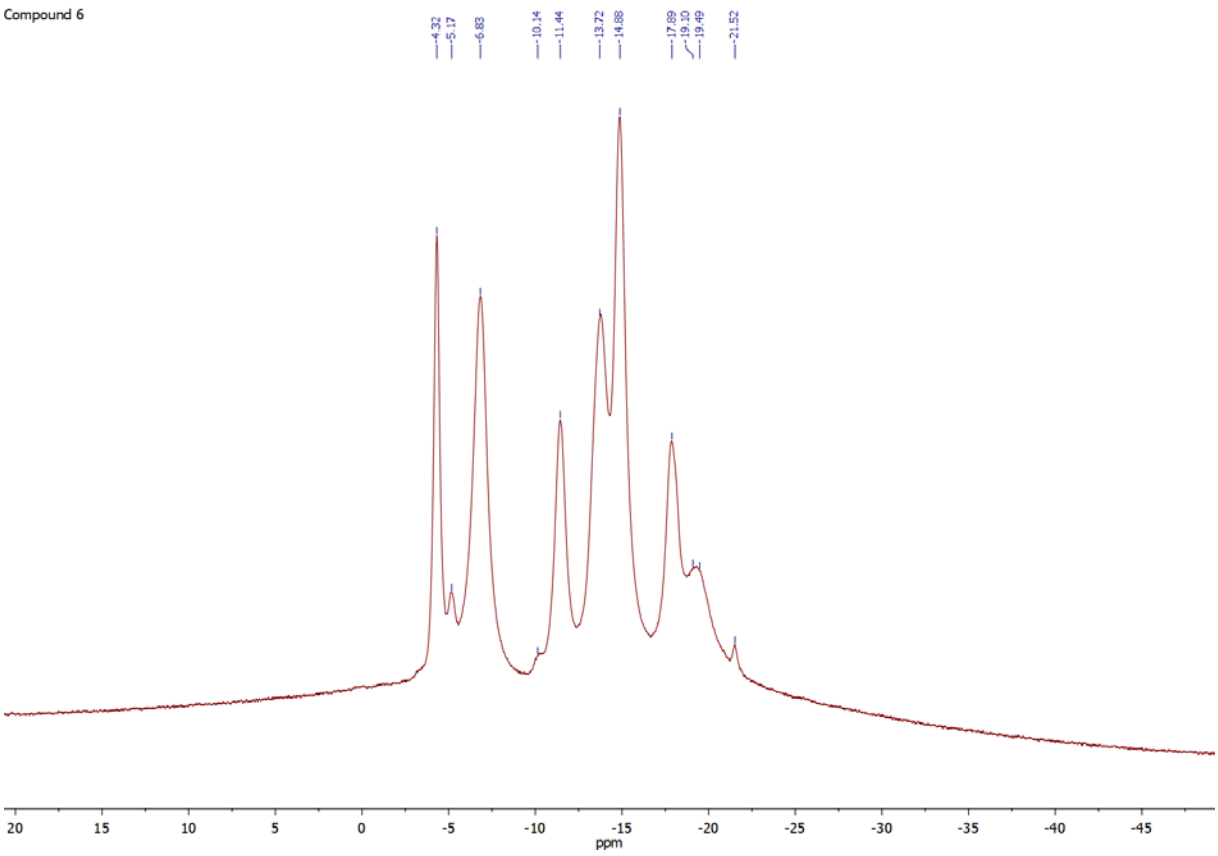


Figure S48: $^{11}B\{^{1}H\}$ NMR spectrum of compound **6**.

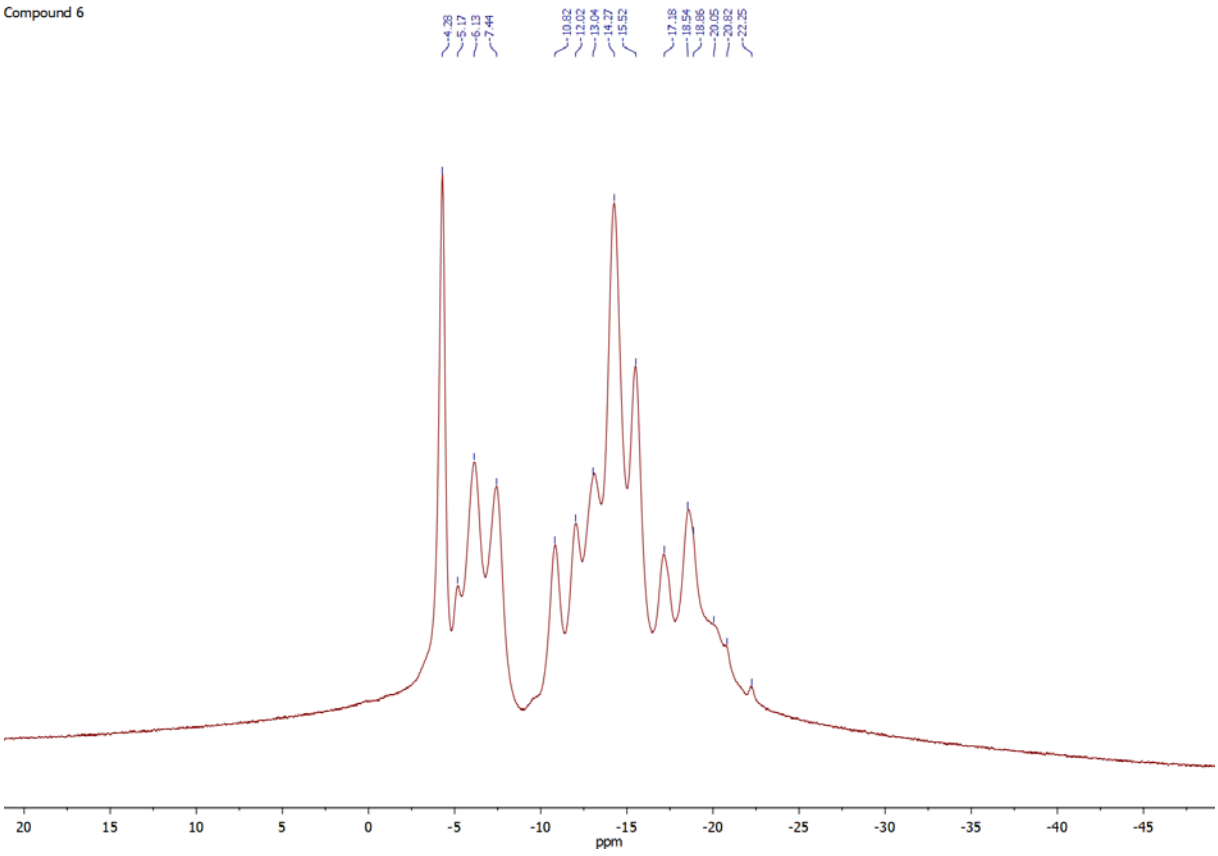


Figure S49: ^{11}B NMR spectrum of compound **6**.

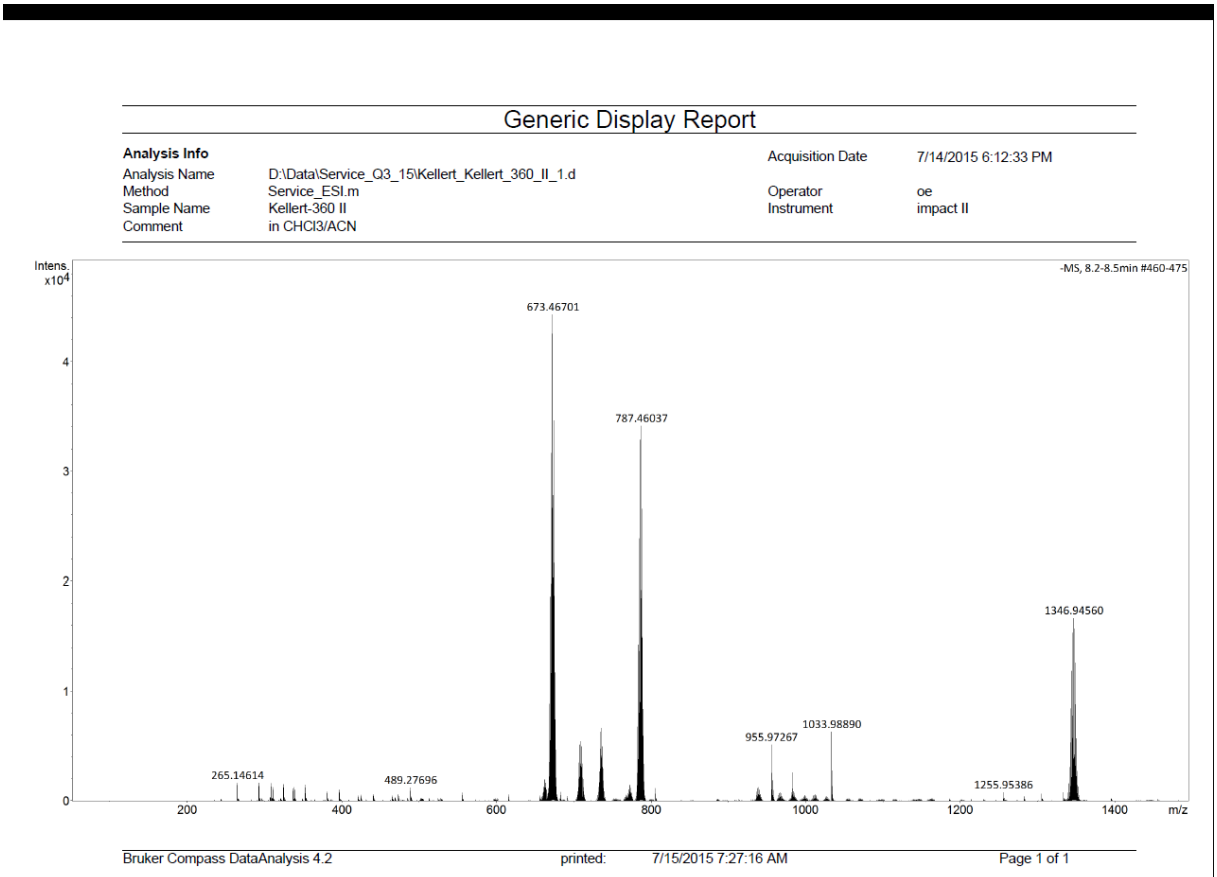


Figure S50: ESI MS (negative mode) of compound **6**.

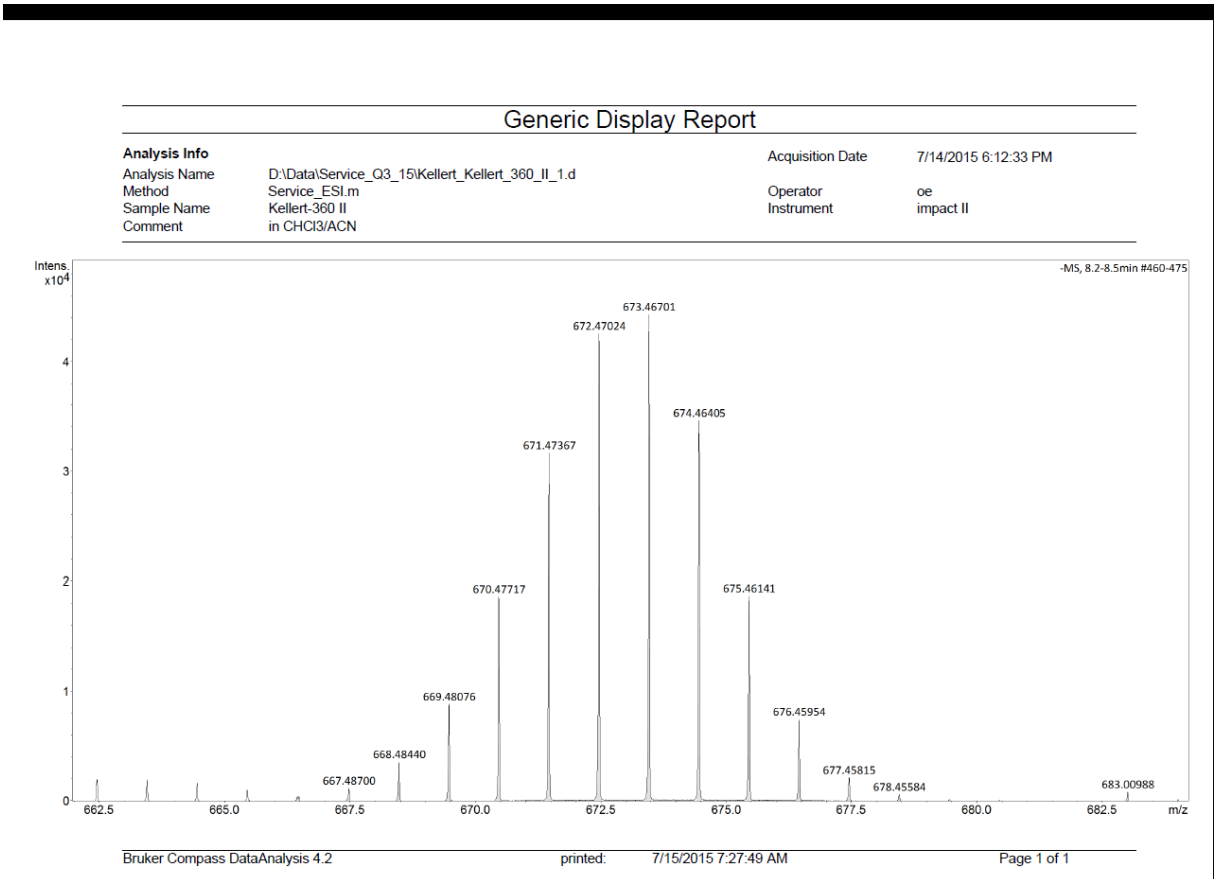


Figure S51: Section of the ESI MS of compound **6**.

8. Synthetic attempts to obtain biscarboranyl-triazine-based carboxylic acids from 3 (see Scheme 1, main text).

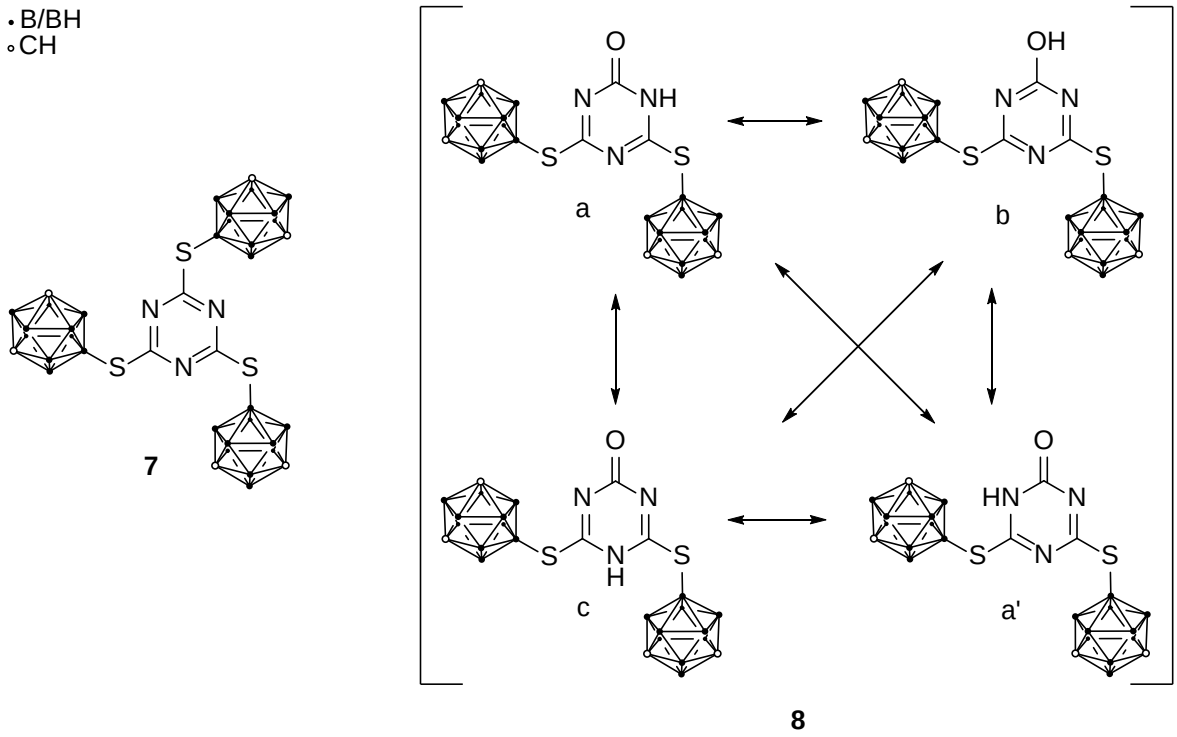
Table S2:

entry	solvent	eq. of Nuc	base[a]	Lewis acid[a]	T	t	result
Thioglycolic acid							
1	MeCN	2.00	DIPEA (5.00)	-	reflux	1 d	n.p.o.
2	MeCN	2.00	DIPEA (4.00)	-	rt	1 d	y.n.d, crystals of **4**
3	MeCN/H_2O (1:1.25)	1.14	NaOH (4.07)	-	85°C	18 h	n.p.o., 8% **7**
4	DCM	1.05	-	$AlCl_3$ (2.10)	reflux	8 h	n.p.o., 94% **3**, 4% **8**
5	DCM	1.20	-	$TiCl_4$ (1.20)	reflux	3 d	n.p.o.
6	MeCN	1.49	DIPEA (4.07)	-	reflux	3 h	27% **4**, 43% **2**
Glycolic acid							
7	MeCN/H_2O (1:1.25)	1.16	NaOH (4.07)	-	85°C	18 h	n.p.o., 20% **7**, 38% **2**
8	acetone (not abs.)	5.18	K_2CO_3 (10.4)	-	reflux	24 h	n.p.o., mixtures of **7** and **8**
Glycine							
9	MeCN/H_2O/EA (3.33:2:1)	1.61	NaOH (5.59)	-	95°C	6 h	60% **5**
10	MeCN	1.55	DIPEA (4.00)	-	reflux	6 h	20% **5**, 23% **2**, 10% **8**
11	MeCN	2.30	NaH (exc.)	-	rt	1 d	n.p.o.
12[b]	MeCN/H_2O (7:3)	1.64/ 1.64/ 1.74	NaOH (3.64/ 3.64/ 3.94)	-	70°C	4 h	27% **5**, mixture of **2** and **3**, 14% **8**
13	acetone (not abs.)	1.51	-	$AgNO_3$ (1.72)	rt	1 d	n.p.o., 94% **3**
14	THF	1.98	-	$AgNO_3$ (3.50)	55°C	3 d	30% **3**, 4% **8**
15	THF	1.68	K_2CO_3 (5.90)	-	reflux	20 h	17% **3**
16	DCM	1.11	-	$AgBF_4$ (1.19)	rt	1 d	91% **3**
***N*α-Boc-L-lysine**							
17	MeCN/H_2O (1:1)	1.15	NaOH (6.38)	-	85°C	6 h	69% **6**
18	MeCN/H_2O (1:1.25)	1.14	NaOH (4.07)	-	85°C	18 h	47% **6**
19	acetone (not abs.)	2.73	K_2CO_3 (10.4)	-	reflux	16 h	41% **6**
20	MeCN/H_2O/ Acetone (4:2:1)	1.42	NaOH (6.87)	-	90°C	6 h	37% **6**, 22% **8**

Nuc = nucleophile; [a] number in brackets is the equivalent of base or Lewis acid compared to **3**; [b] one reaction split into three batches; y.n.d. = yield not determined; DIPEA = *N*,*N*-diisopropylethylamine, reflux = T_b of the given solvent or solvent mixture; n.p.o. = no product obtained; MeCN = acetonitrile, DCM = dichloromethane, EA = ethyl acetate, THF = tetrahydrofuran.

9. Formation and characterisation of by-products 7 and 8

Two by-products were obtained, the tris-carboranyl-*s*-triazine derivative 2,4,6-tris(1,7-dicarba-*closo*-dodecaboran-9-ylthio)-1,3,5-triazine (**7**) (in 8 to 20% yield) and the hydrolysis product of **3**, namely 4,6-bis(1,7-dicarba-*closo*-dodecaboran-9-ylthio)-1,3,5-triazine-2(1*H*)-one (**8**) (in 4 to 22% yield). **7** and **8** were characterised by NMR spectroscopy, mass spectrometry, infrared spectroscopy, elemental analysis and single crystal X-ray diffraction measurements. Scheme S1 gives the structure of **7** and the tautomers of **8**.



Scheme S1: By-products **7** and **8**; tautomers of **8** are shown.

First, the formation of the trisubstituted triazine **7** was unclear, but the observation of free **2** in some reactions after work-up indicated cleavage of the carbon–sulfur bond in **3** under basic conditions (see Table S1). The free thiol is a very good nucleophile and can attack the C–Cl bond in **3**, giving compound **7**.[2]

Subsequently, computations were carried out with ORCA 3.0.2.[3] Geometry optimisations in the gas phase were carried out with the TPSSh hybrid functional[4] using the def2-TZVPP basis set.[5] Density fitting techniques, also called resolution-of-identity approximation (RI), were used to speed up the geometry optimisations.[6] All figures were rendered with the UCSF Chimera package.[7] The contributions of atomic orbitals to the molecular orbitals were derived from Loewdin population analyses. Figure S52 shows the optimised geometry, lowest unoccupied molecular orbital (LUMO) and LUMO+1 of compound **3**. The largest contribution to the LUMO

of **3** comes from p_z orbitals at C5 and C6 (22.7% and 14.0%, respectively; using the numbering scheme in Figure 3 main text or Figure S 21). The p_z orbital of C7 contributes only 0.8% to the LUMO. Furthermore, two sulfur atoms also contribute to the LUMO of **3** (S1: 4.0% p_z and S2: 3.0% p_z) resulting in a C5–S1 and C6–S2 antibonding character. Based on these results, a nucleophilic attack is more likely at position C5 or C6 than at C2. These computational results support the observation of by-product **7** and the formation of small amounts of **2**.

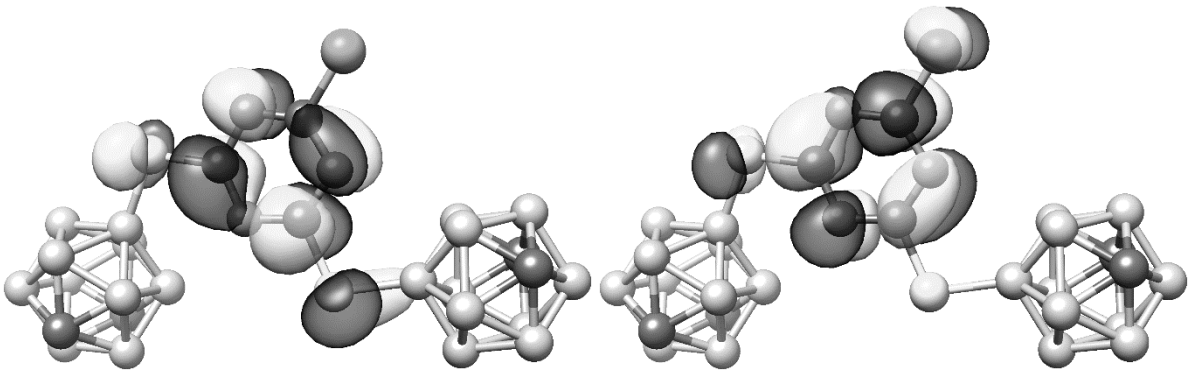
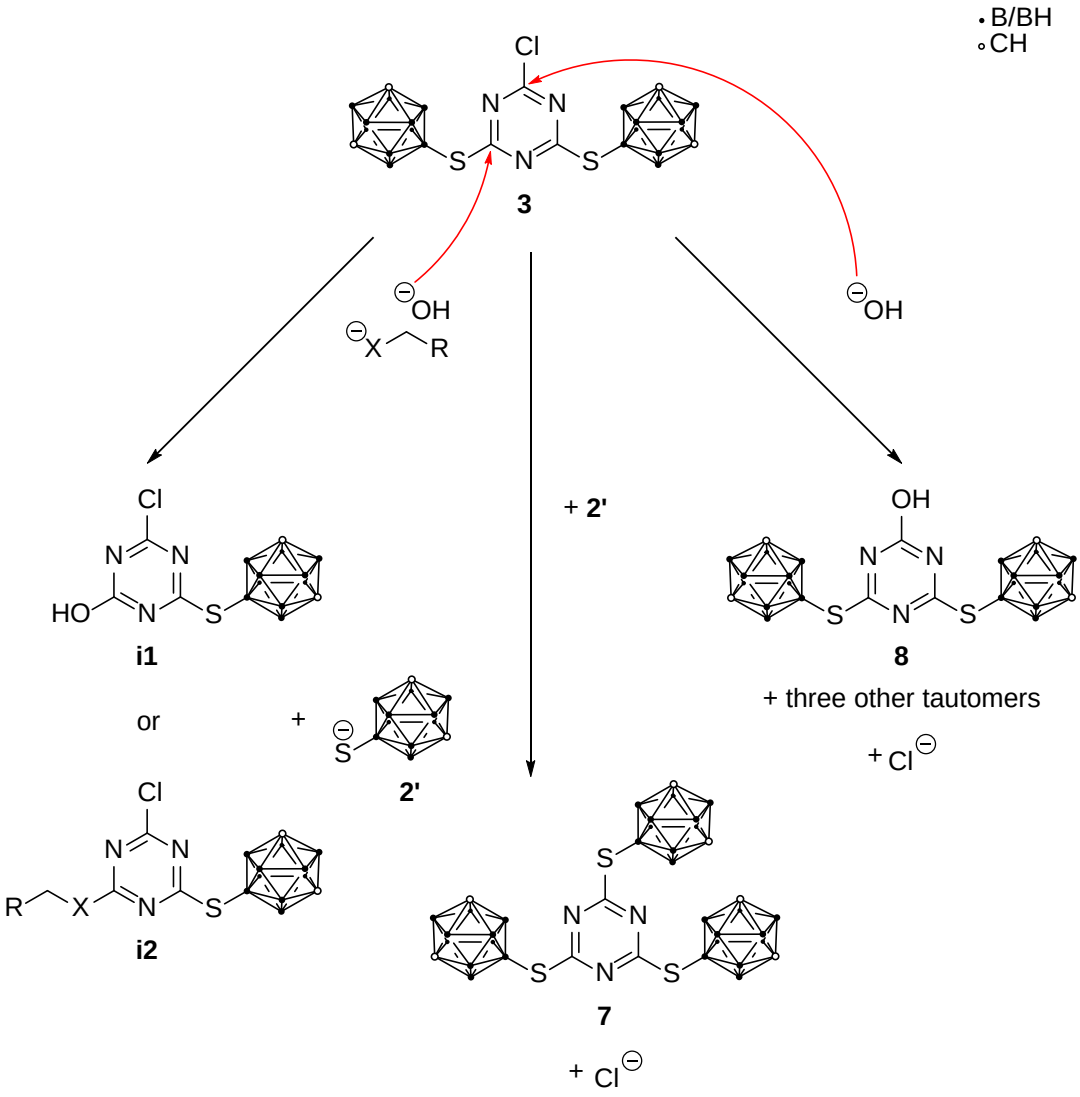


Figure S52: RI-TPSSh/def2-TZVPP optimised geometry, LUMO (left) and LUMO+1 (right) of **3** in the same orientation as in Figure 3 (main text) or Figure S21. Hydrogen atoms are not shown for clarity. MO surface isovalue: 0.03.

The formation of the by-product **8** is due to hydrolysis of the C–Cl bond in **3** (see Table S2). This seems to be a competing reaction in comparison to the nucleophilic attack at the C–S bond described above. The largest contribution to the LUMO+1 of **3** comes from C7 p_z orbitals (25.0%). Cl1 directly bonded to C7 also contributes to the LUMO+1 (3.9% p_z) resulting in a C7–Cl1 antibonding character. However, one of the sulfur atoms also contributes to the LUMO+1 of **3** (S2: 2.2% p_z) resulting in a C6–S2 antibonding character. Since LUMO+1 of **3** is only 0.05 eV higher than the corresponding LUMO, a competition between the hydrolysis of the C7–Cl1 and the C–S bonds cannot be excluded, in agreement with the experimental observation of by-product **8**.

The hydrolysis of cyanuric chloride under aqueous basic conditions to give the respective cyanuric or isocyanuric acid was already investigated.[8] Here, no attempts were made to find conditions that favour one of the two by-products. However, it was observed that **7** and **8** were formed when basic aqueous conditions were employed during the reaction or work-up. It is assumed that **7** is formed during the reaction, and **8** is mainly formed during the work-up or when excess of sodium hydroxide was used in aqueous media (Scheme S2). Therefore, for targeted synthesis, **7** should be prepared from cyanuric chloride and excess of **2** under anhydrous, basic conditions and elevated temperatures, while for **8**, hydrolysis of **3** with excess of sodium hydroxide in aqueous solution should be employed.

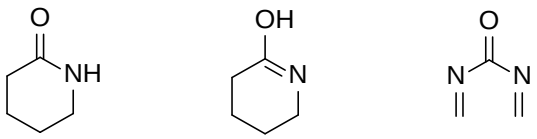


X = NH, O, S
R = COOH, $(CH_2)_3CH(NHC(O)O^tBu)COOH$

Scheme S2: Reaction pathways leading to **7** and **8**; left: attack at the C–S bond by a nucleophile; right: hydrolysis of the C–Cl bond with excess of hydroxide under aqueous conditions.

In the solid state, of the tautomers of **8** the lactam structure (a and a', Scheme S1) is favoured over the lactim structure (b, Scheme S1) and the urea structure (c, Scheme S1), structural motifs are also shown in Figure S53; this was confirmed by structure determination of single crystal obtained from two independent reactions. In one type of crystals obtained from acetone, one molecule of **8** forms an adduct with acetone; in the other type of crystals, obtained from methanol, two molecules of **8** form a dimer. Compound **8** represents an interesting molecule

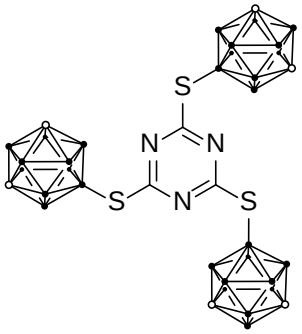
with its different tautomers. As a lactam derivative (a and a', Scheme S1), **8** could also possess bioactive properties,[9] which could be topic of further research.



A **B** **C**

Figure S53: A) Lactam motif, B) lactim motif, C) 1,3-dimethylene urea motif.

Characterisation of 2,4,6-tris(1,7-dicarba-*closo*-dodecaboran-9-ylthio)-1,3,5-triazine (7)



7

T_m: 173-175 °C (toluene, decomposition). IR (KBr): $\tilde{\nu}$ = 3423 (w), 3059 (m), 2921 (m), 2851 (w), 2603 (s), 2386 (w), 2082 (w), 1718 (w), 1527 (w), 1469 (s), 1313 (w), 1241 (s), 1156 (m), 1103 (w), 1064 (m), 990 (m), 951 (m), 864 (m), 841 (s), 791 (w), 757 (w), 729 (m), 625 (w) cm^{-1}. ^1H NMR (400.16 MHz, acetone-d_6): δ = 1.38 − 3.62 (m, br[a], 27 H, $B_{10}H_9$), 3.77 (s, br, 6 H, CH) ppm. $^{13}C\{^1H\}$ NMR (100.63 MHz, acetone-d_6): δ = 55.9 (s, CH, CH), 179.3 (s, C_q, CS) ppm. $^{11}B\{^1H\}$ NMR (128.38 MHz, acetone-d_6): δ = −18.3 (s, br, 3 B), −16.9 (s, 3 B), −14.0 (s, 6 B), −12.7 (s, br, 6 B), −10.4 (s, 3 B), −5.9 (s, br, 6 B), −3.7 (s, 3 B, BS) ppm. ^{11}B NMR (128.38 MHz, acetone-d_6): δ = −15.5 (m, br, 18 B), −10.4 (d, $^1J_{BH}$ = 152 Hz, 3 B), −5.9 (d, br, $^1J_{BH}$ = 167 Hz, 6 B), −3.7 (s, 3 B, BS) ppm. ESI MS: positive mode, $C_9H_{34}B_{30}N_3S_3$, m/z calculated: 605.5, found: 605.5 (100%, $[M+H]^+$), $NaC_9H_{33}B_{30}N_3S_3$, m/z calculated: 627.5, found: 627.5 (12%, $[M+Na]^+$), $NaC_{18}H_{66}B_{60}N_6S_6$, m/z calculated: 1231.0, found: 1231.0 (9%, $[2M+Na]^+$).

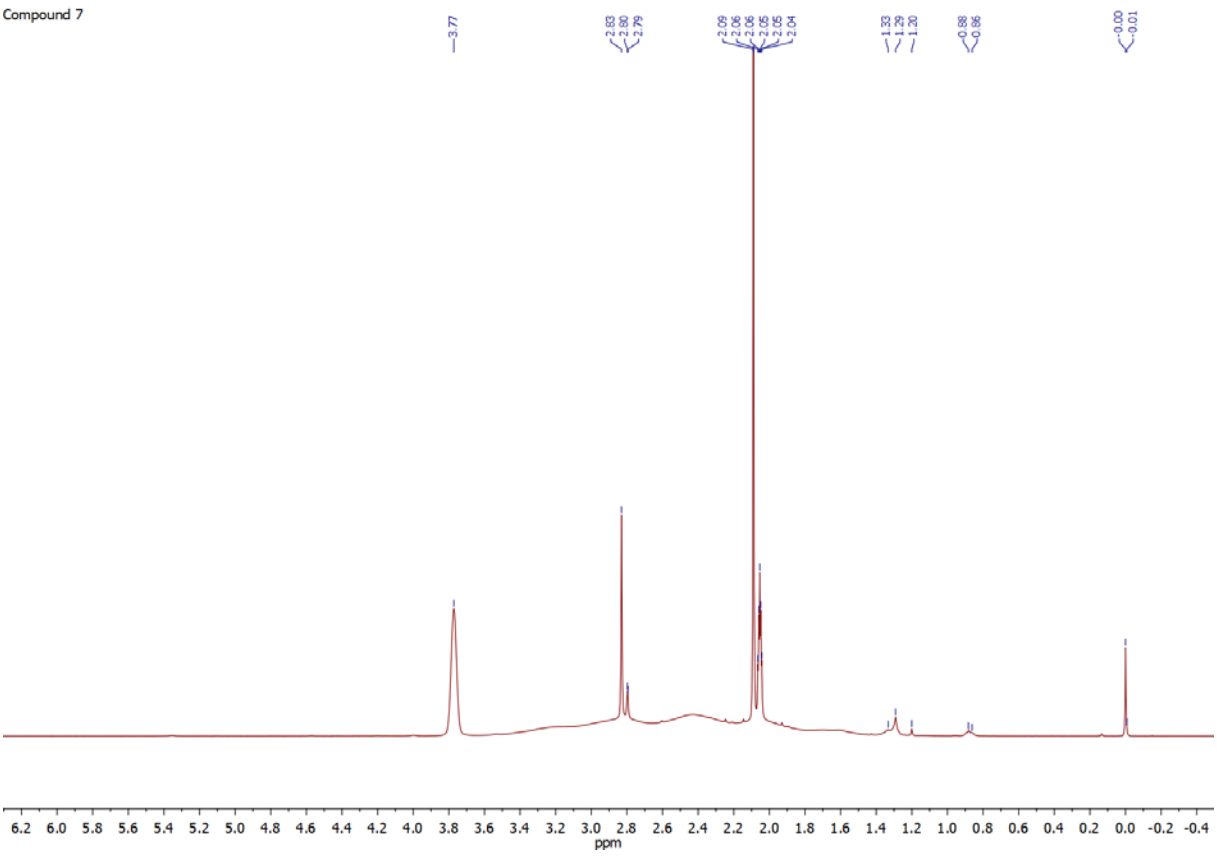


Figure S54: ^{1}H NMR spectrum of compound **7** with acetone and water as minor impurities.

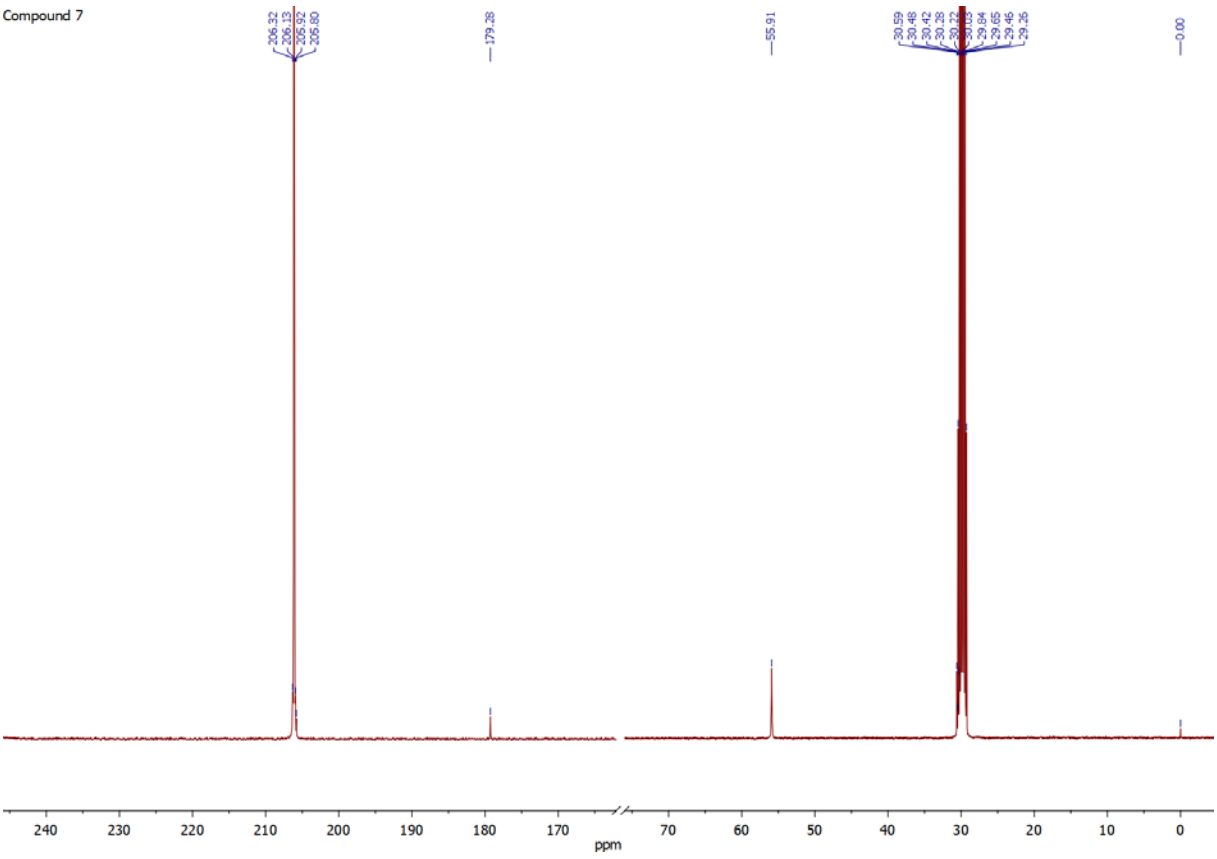


Figure S55: $^{13}C\{^{1}H\}$ NMR spectrum of compound **7**.

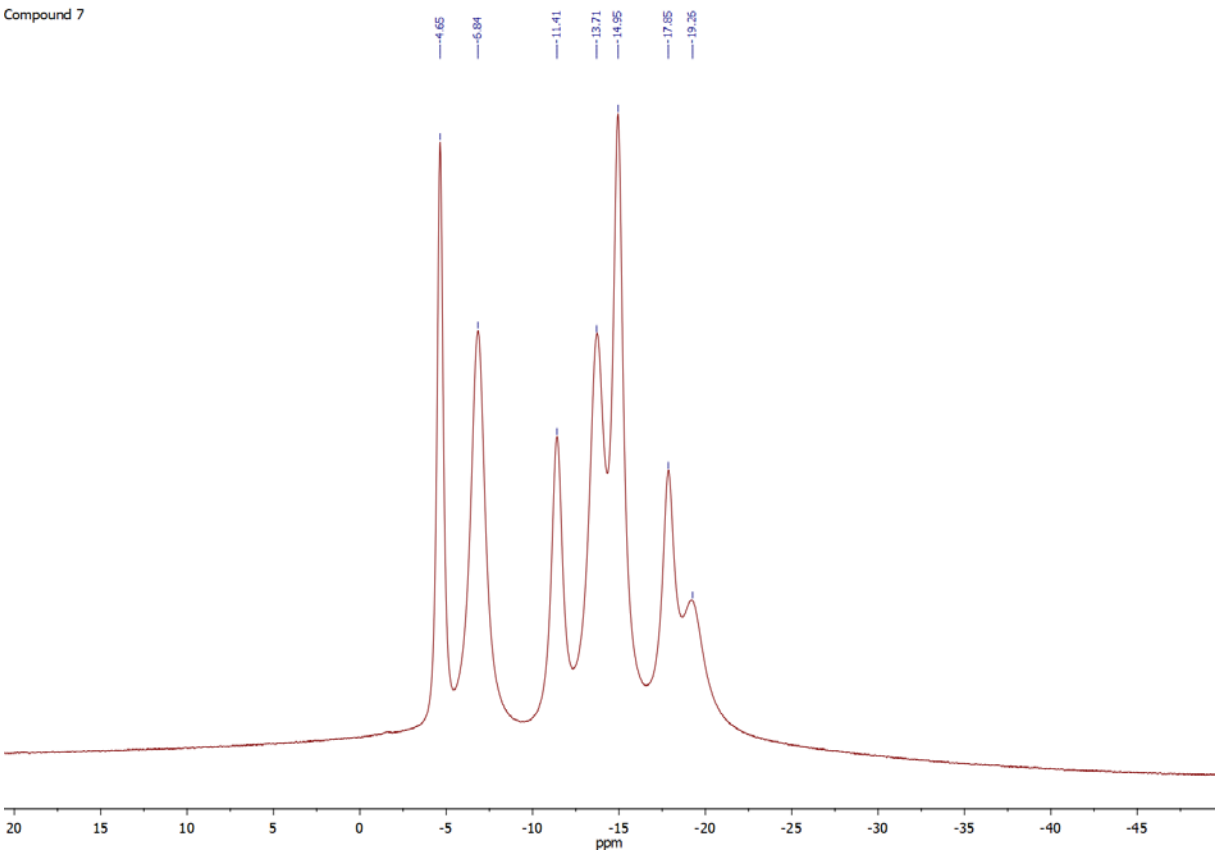


Figure S56: $^{11}B\{^{1}H\}$ NMR spectrum of compound **7**.

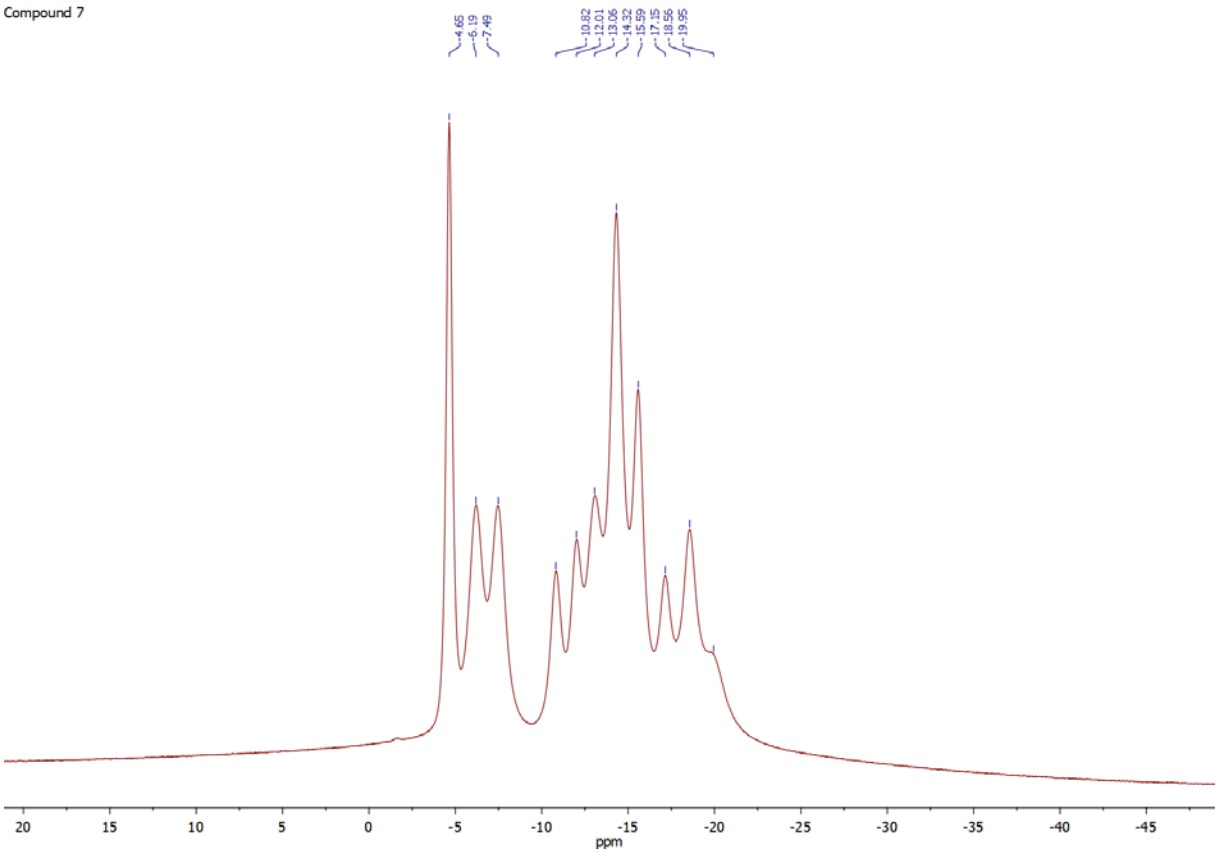


Figure S57: ^{11}B NMR spectrum of compound **7**.

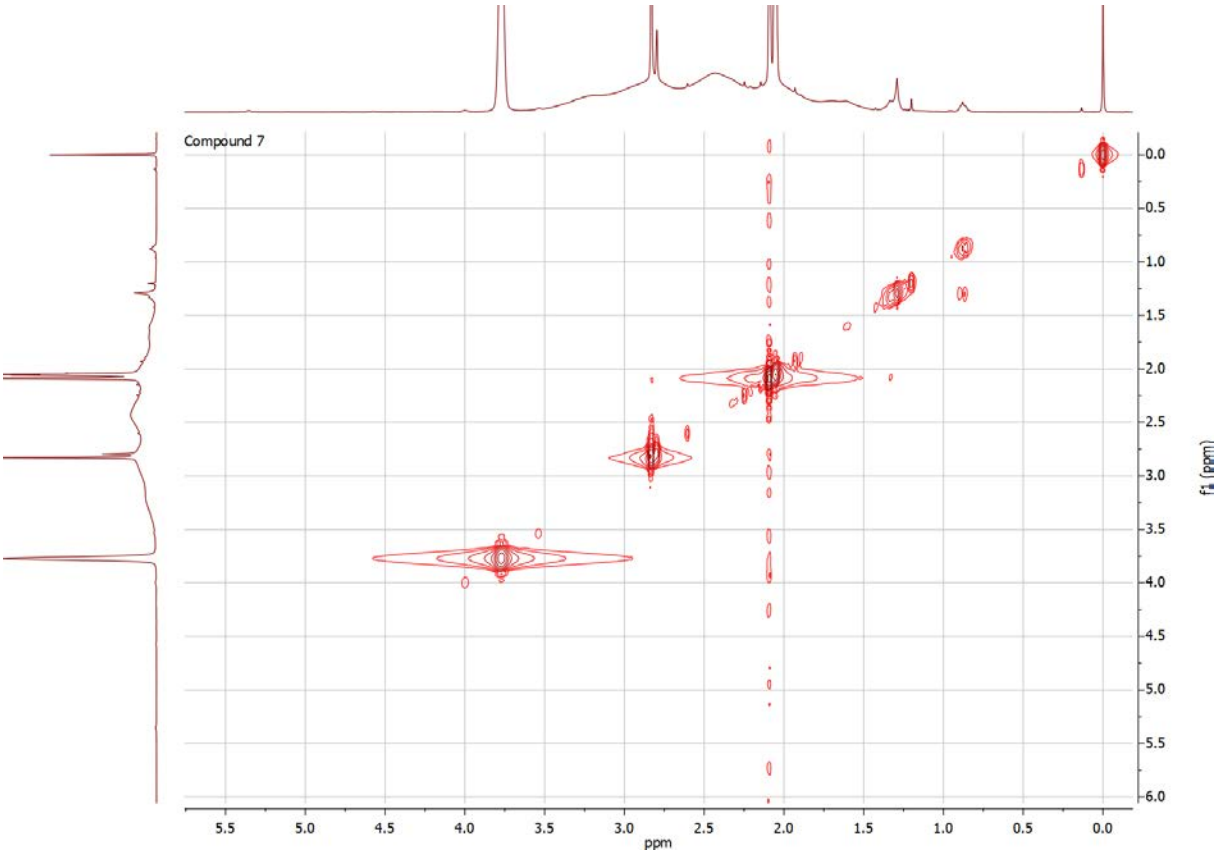


Figure S58: ^{1}H-^{1}H-COSY spectrum of compound **7**.

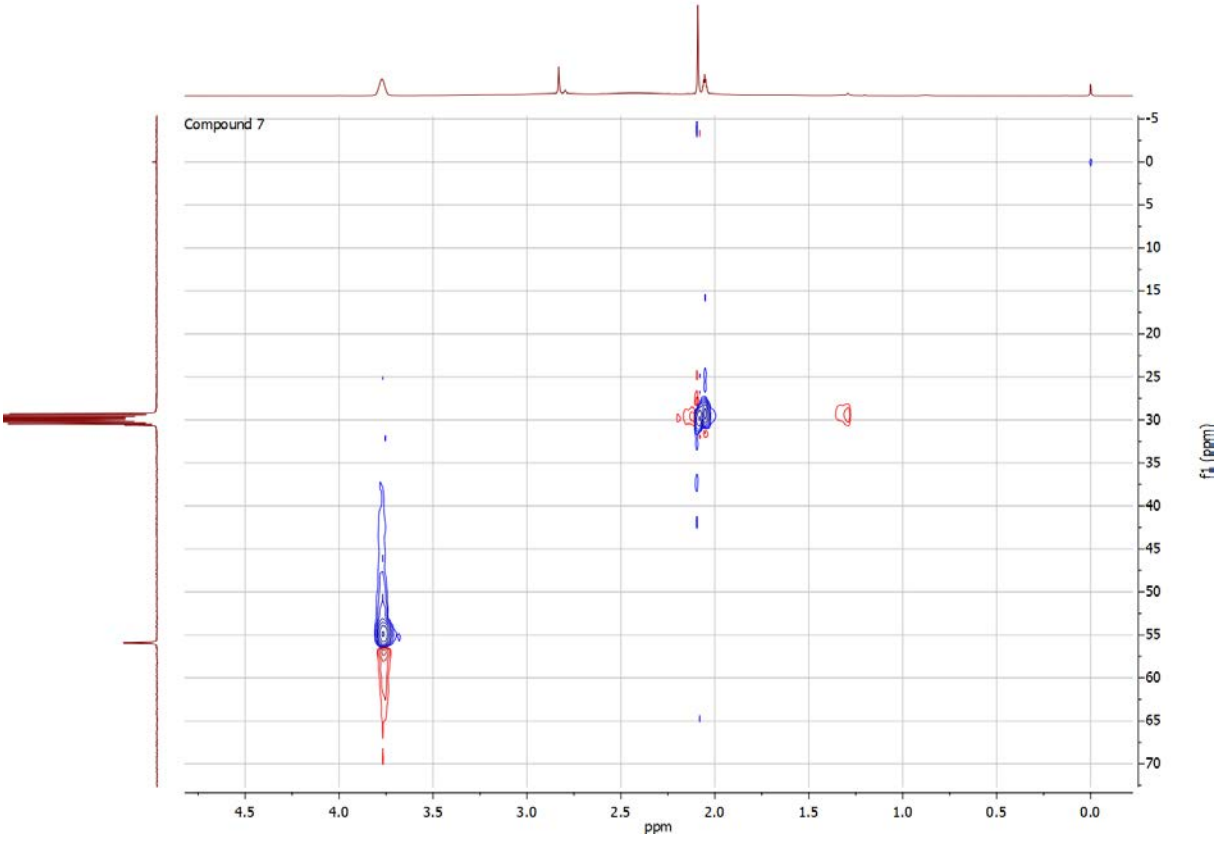


Figure S59: ^{1}H-^{13}C-HSQC spectrum of compound **7**.

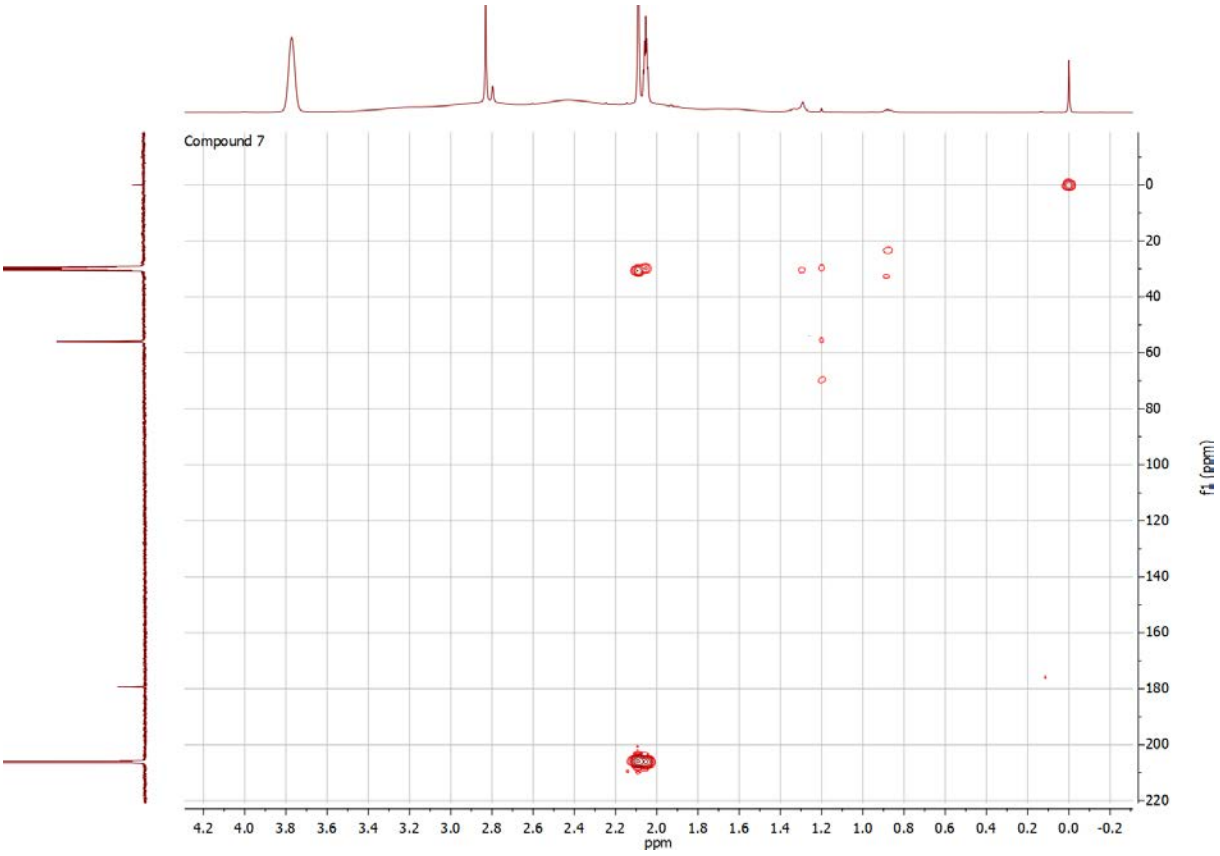


Figure S60: ^{1}H-^{13}C-HMBC spectrum of compound **7**.

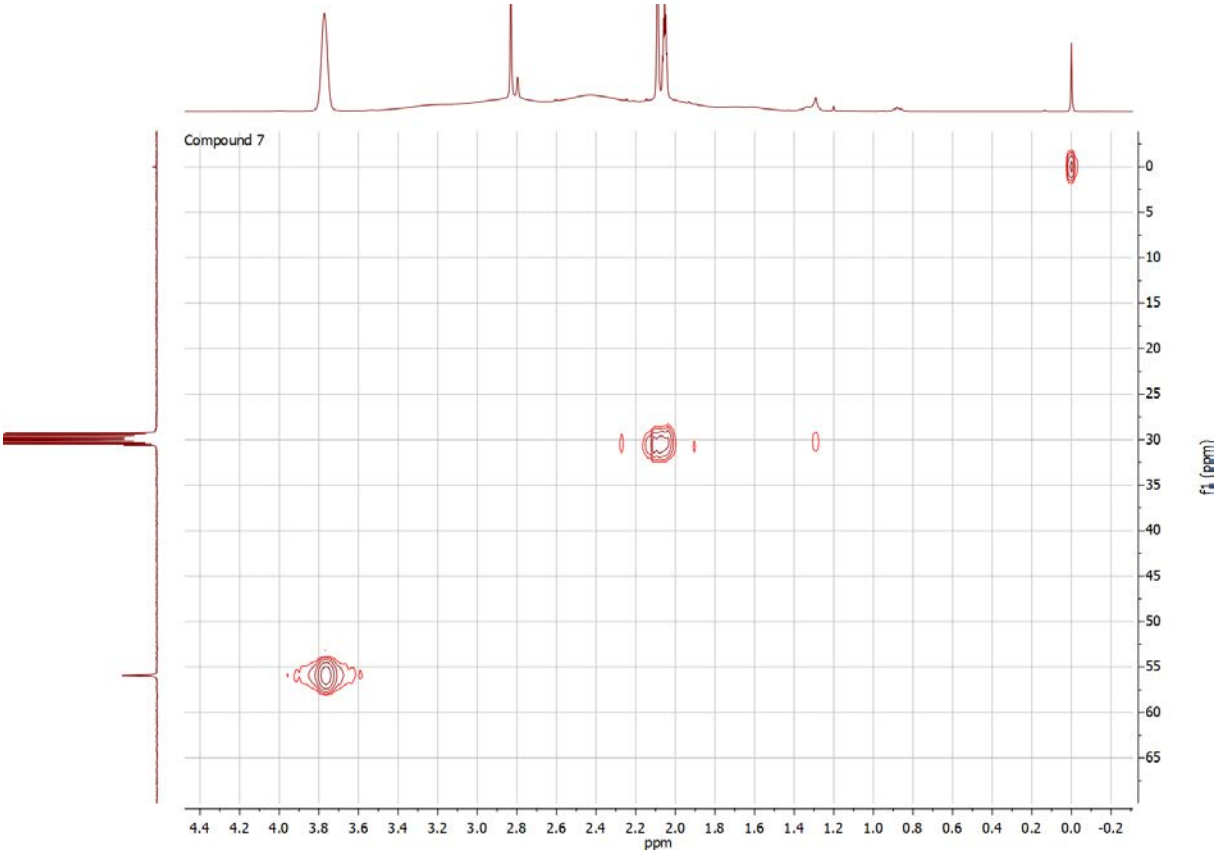


Figure S61: ^{1}H-^{13}C-HMQC spectrum of compound **7**.

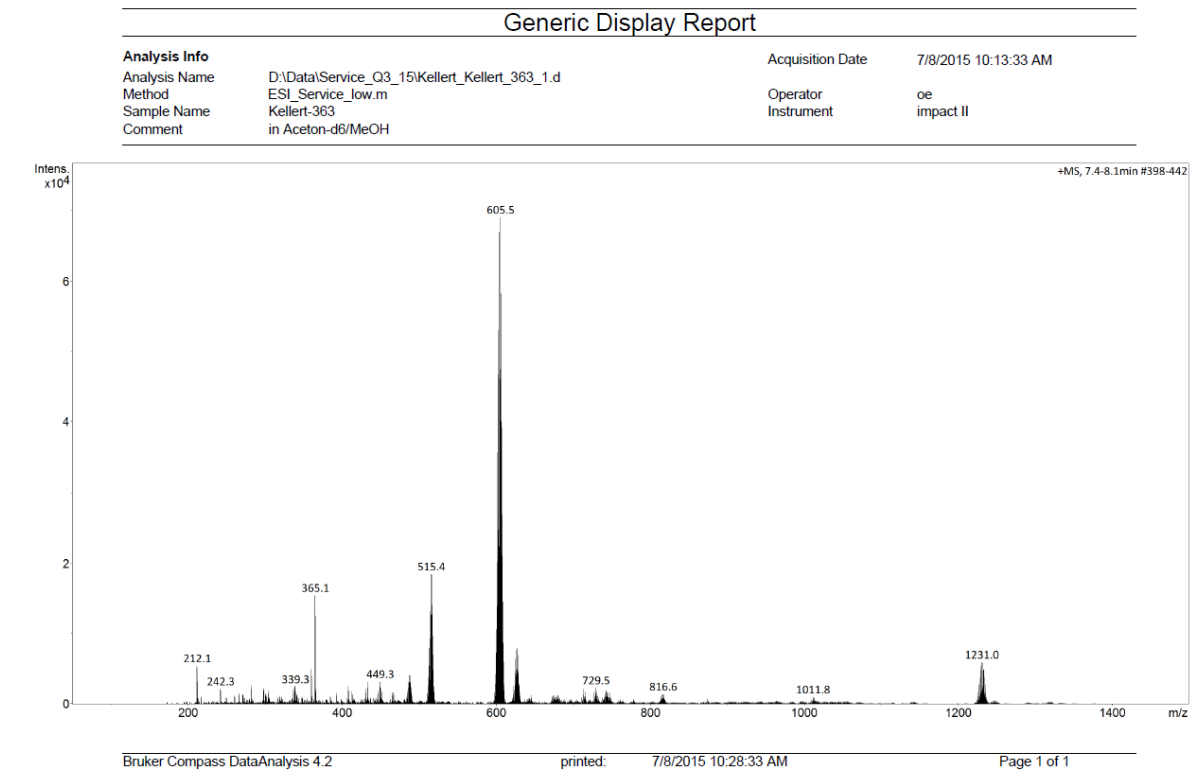


Figure S62: ESI MS (positive mode) of compound **7**.

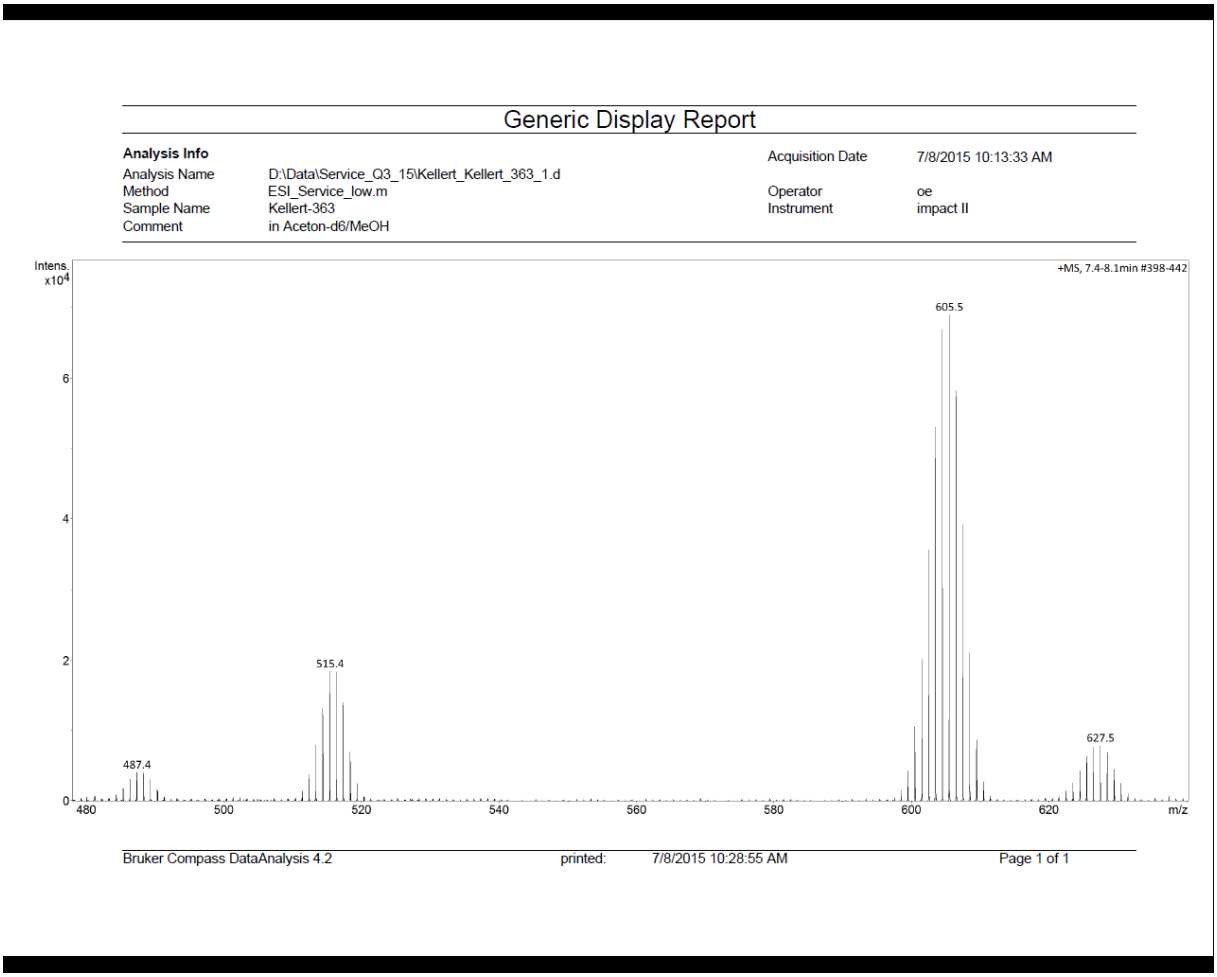


Figure S63: Section of the ESI MS of compound **7**.

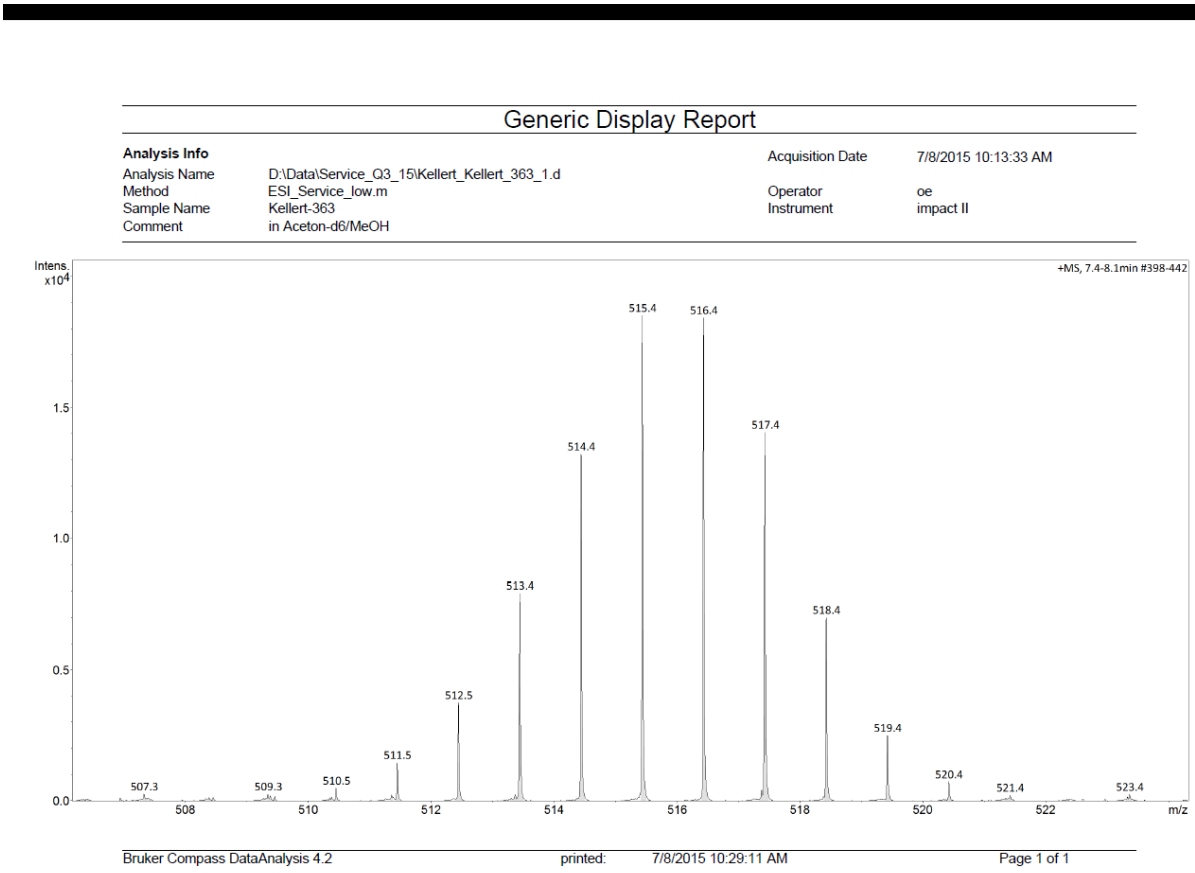


Figure S64: Section of the ESI MS of compound **7**.

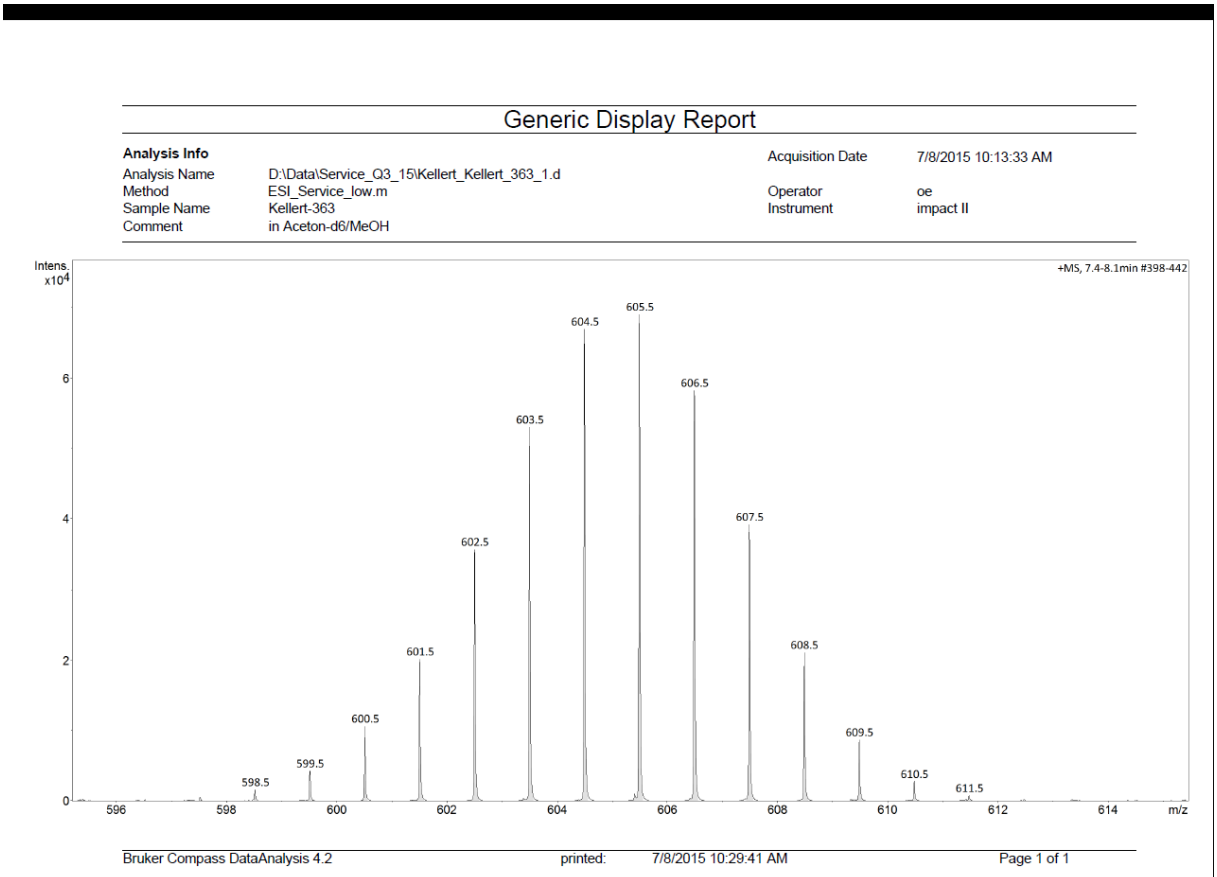


Figure S65: Section of the ESI MS of compound **7**.

Crystallographic data of 7

Empirical formula	$C_{23}H_{49}B_{30}N_3S_3$
Formula weight	788.13
Temperature	130(2) K
Wavelength	71.073 pm
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	a = 1085.25(4) pm α = 104.021(3)°
	b = 1278.93(5) pm β = 95.652(3)°
	c = 1797.49(5) pm γ = 113.340(4)°
Volume	2.1688(2) nm^3
Z	2
Density (calculated)	1.207 Mg/m^3
Absorption coefficient	0.198 mm^{-1}
F(000)	812
Crystal size	0.4 x 0.3 x 0.2 mm^3
Theta range for data collection	1.823 to 32.533°
Index ranges	$-16 \leq h \leq 16$, $-18 \leq k \leq 19$, $-27 \leq l \leq 27$
Reflections collected	40159
Independent reflections	14365 [R(int) = 0.0299]
Completeness to theta = 30.510°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.97860
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	14365 / 45 / 690
Goodness-of-fit on F^2	1.029
Final R indices [I>2σ(I)]	R_1 = 0.0517, wR_2 = 0.1261
R indices (all data)	R_1 = 0.0754, wR_2 = 0.1401
Residual electron density	1.321 and –0.483 $e \cdot Å^{-3}$

Comments: Structure solution with SHELXT-2014 (dual-space method). Anisotropic refinement of all non-hydrogen atoms, except the minor disordered 16% part of the toluene molecule and toluene molecules disordered on a centre of inversion, with SHELXL-2018. Excluding disordered parts of the structure, all H atoms were located on difference Fourier

maps calculated at the final stage of the structure refinement. Carborane carbon atoms could be localised with a bond length and displacement parameter analysis. Three disordered toluene molecules. Two of them are located on a special position (centre of inversion) and the third (C10 to C16) is disordered with a ratio of 0.844(3):0.156(3).

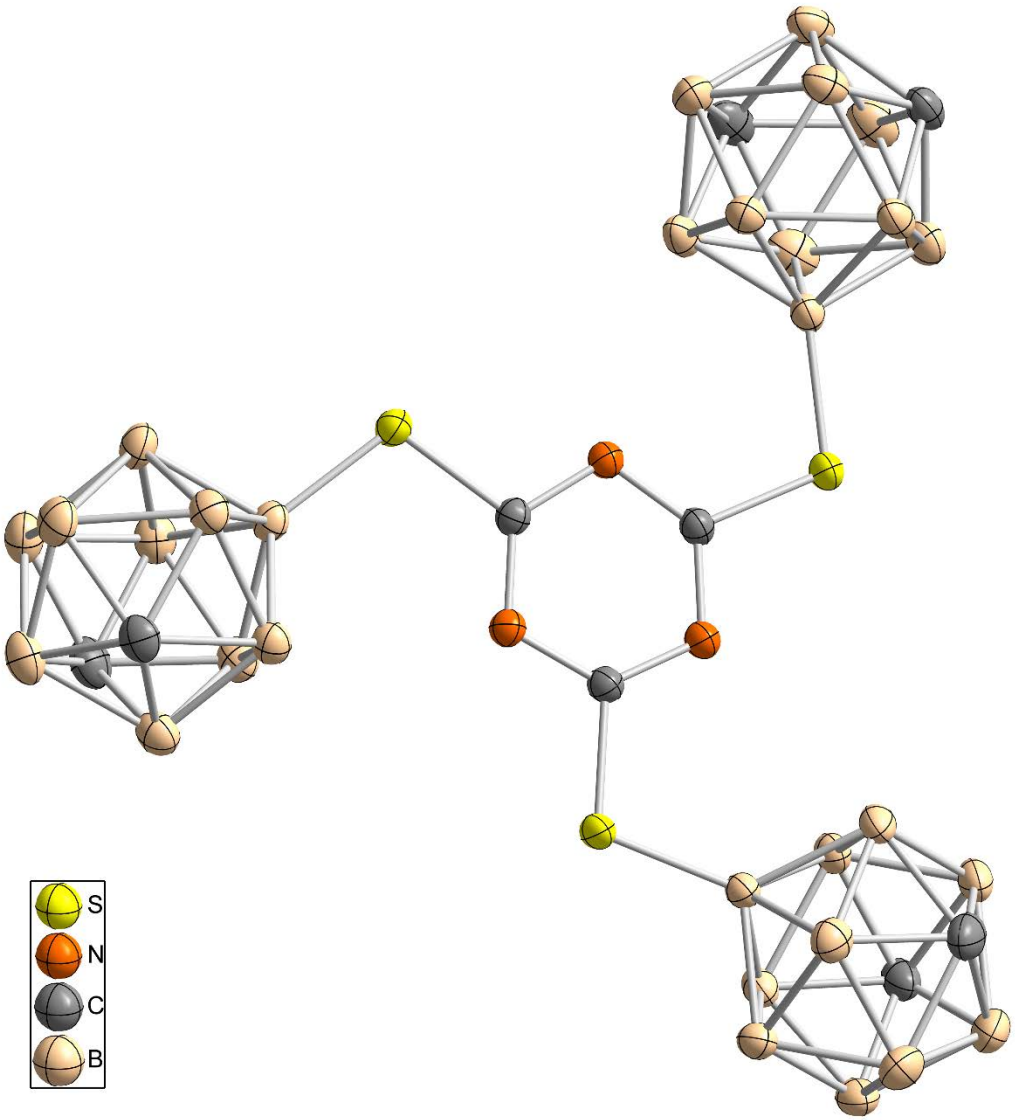
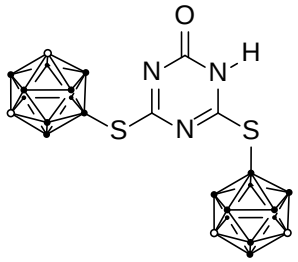


Figure S66: Molecular structure of **7**. Thermal ellipsoids are drawn at the 50% probability level. Solvent molecules and hydrogen atoms are omitted for clarity.

Characterization of 4,6-bis(1,7-dicarba-*closo*-dodecaboran-9-ylthio)-1,3,5-triazine-2(1*H*)-one (8)



8

T_m: 281-283 °C (acetone). IR (KBr): ṽ = 3855 (w), 3631 (w), 3054 (s), 2963 (m), 2610 (s), 2346 (m), 2154 (w), 1880 (w), 1760 (s), 1715 (s), 1650 (s), 1589 (m), 1532 (s), 1403 (s), 1267 (s), 1226 (s), 1147 (m), 1054 (m), 1019 (m), 1008 (m), 949 (m), 917 (m), 850 (s), 805 (m), 794 (m), 758 (m), 731 (m), 674 (w), 665 (w), 613 (m), 598 (m), 468 (m), 450 (m) cm^{-1}. ^1H NMR (400.16 MHz, acetone-*d*$_6$): δ = 1.47 − 3.53 (m, br[a], 18 H, $B_{10}H_9$), 3.78 (s, br, 4 H, CH), 11.0 (s, vbr, 1 H, NH) ppm. $^{13}C\{^1H\}$ NMR (100.63 MHz, acetone-*d*$_6$): δ = 56.0 (s, CH), 153.7 (s, C_q, CO), 164.6, 164.8 (s, C_q, CS) ppm. $^{11}B\{^1H\}$ NMR (128.38 MHz, acetone-*d*$_6$): δ = −18.2 (s, br, 2 B), −16.9 (s, 2 B), −14.0 (s, 4 B), −12.8 (s, br, 4 B), −10.5 (s, 2 B), −6.0 (s, br, 4 B), −4.1 (s, 2 B, BS) ppm. ^{11}B NMR (128.38 MHz, acetone-*d*$_6$): δ = −17.5 (m, br, 4 B), −13.4 (m, br, 8 B), −10.5, (d, $^1J_{BH}$ = 152 Hz, 2 B), −5.9 (d, $^1J_{BH}$ = 167 Hz, 4 B), −4.1 (s, 2 B, BS) ppm. ESI MS: positive mode, $C_7H_{24}B_{20}N_3OS_2$, m/z calculated: 447.3, found: 447.3 (100%, $[M+H]^+$), $NaC_7H_{23}B_{20}N_3OS_2$, m/z calculated: 469.3, found: 469.3 (87%, $[M+Na]^+$), $NaC_{14}H_{46}B_{40}N_6O_2S_4$, m/z calculated: 914.6, found: 914.6 (48%, $[2M+Na]^+$), $KC_7H_{23}B_{20}N_3OS_2$, m/z calculated: 485.3, found: 485.3 (23%, $[M+K]^+$), negative mode, $C_7H_{22}B_{20}N_3OS_2$, m/z calculated: 445.3, found: 445.3 (100%, $[M-H]^-$).

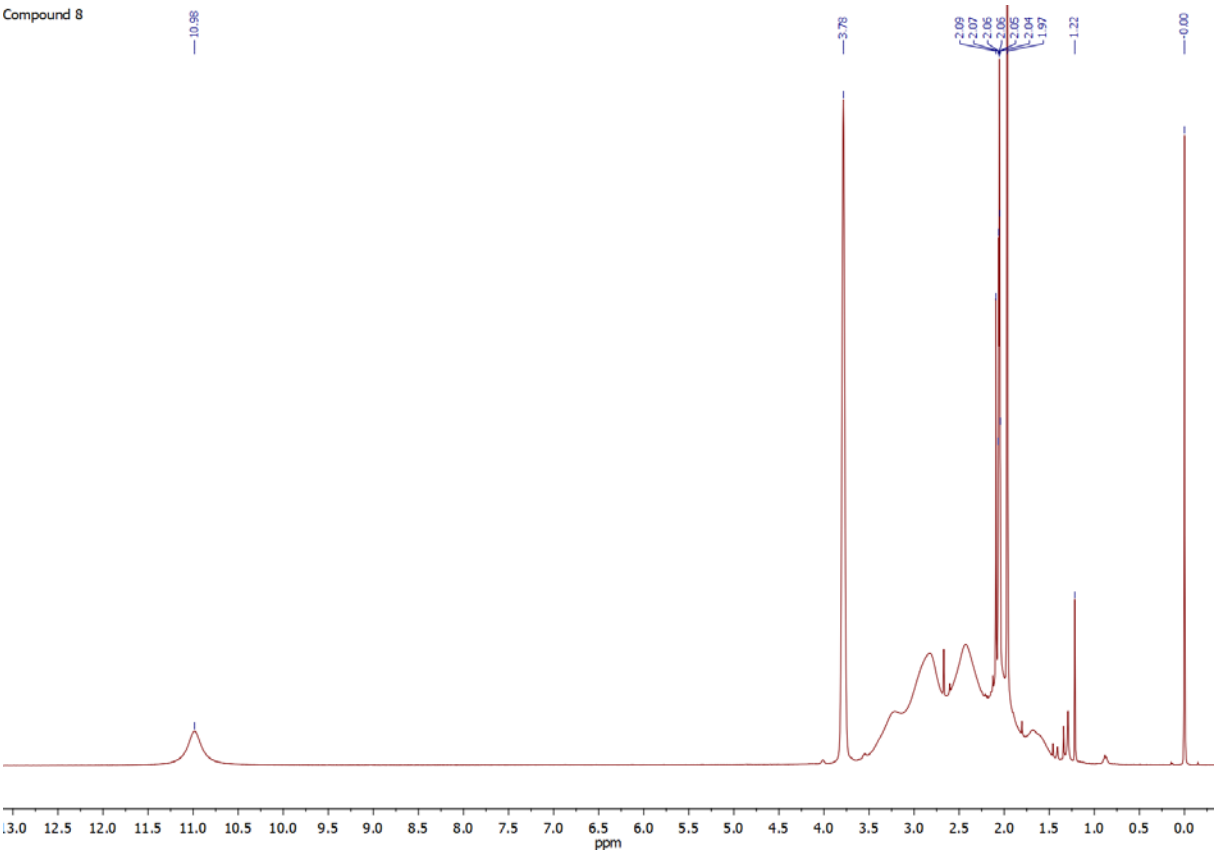


Figure S67: ^{1}H NMR spectrum of compound **8** with acetic acid as a minor impurity.

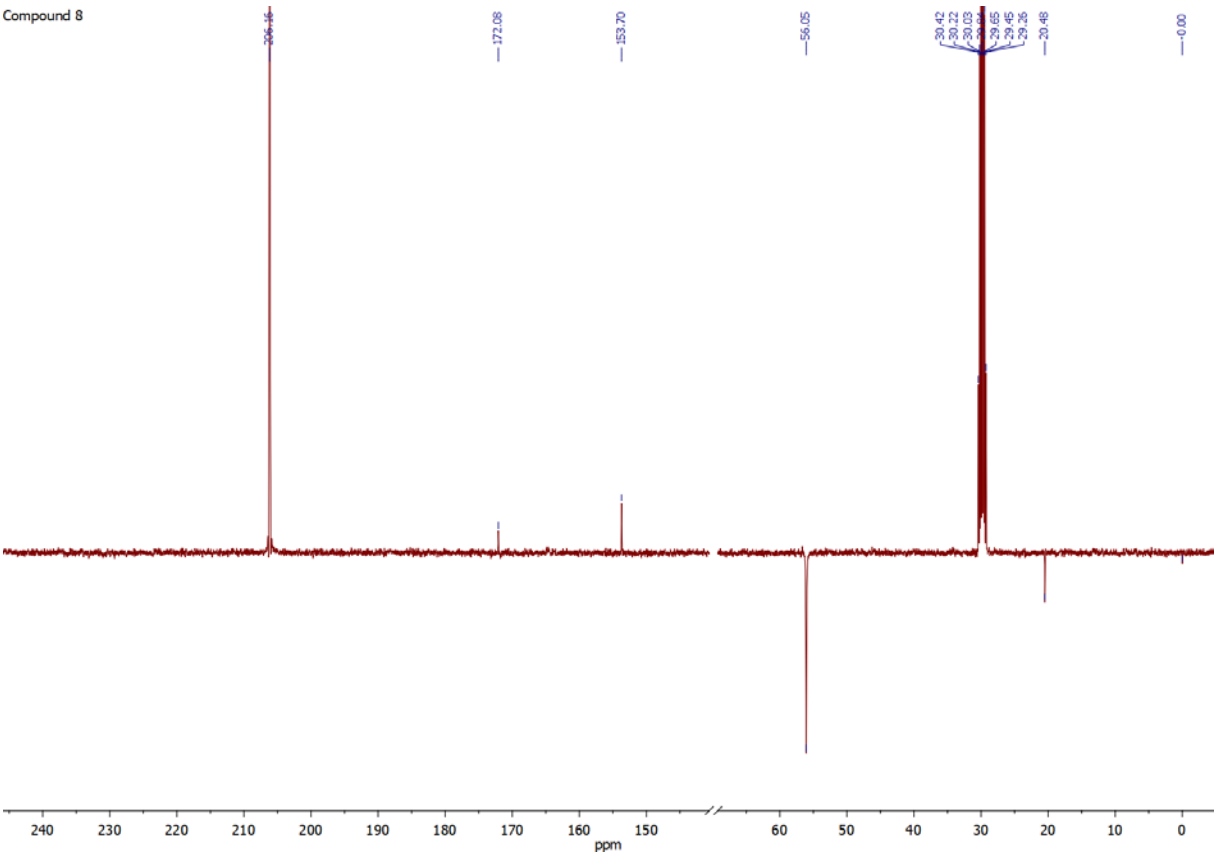


Figure S68: ^{13}C{^{1}H} NMR spectrum of compound **8** with acetic acid as a minor impurity.

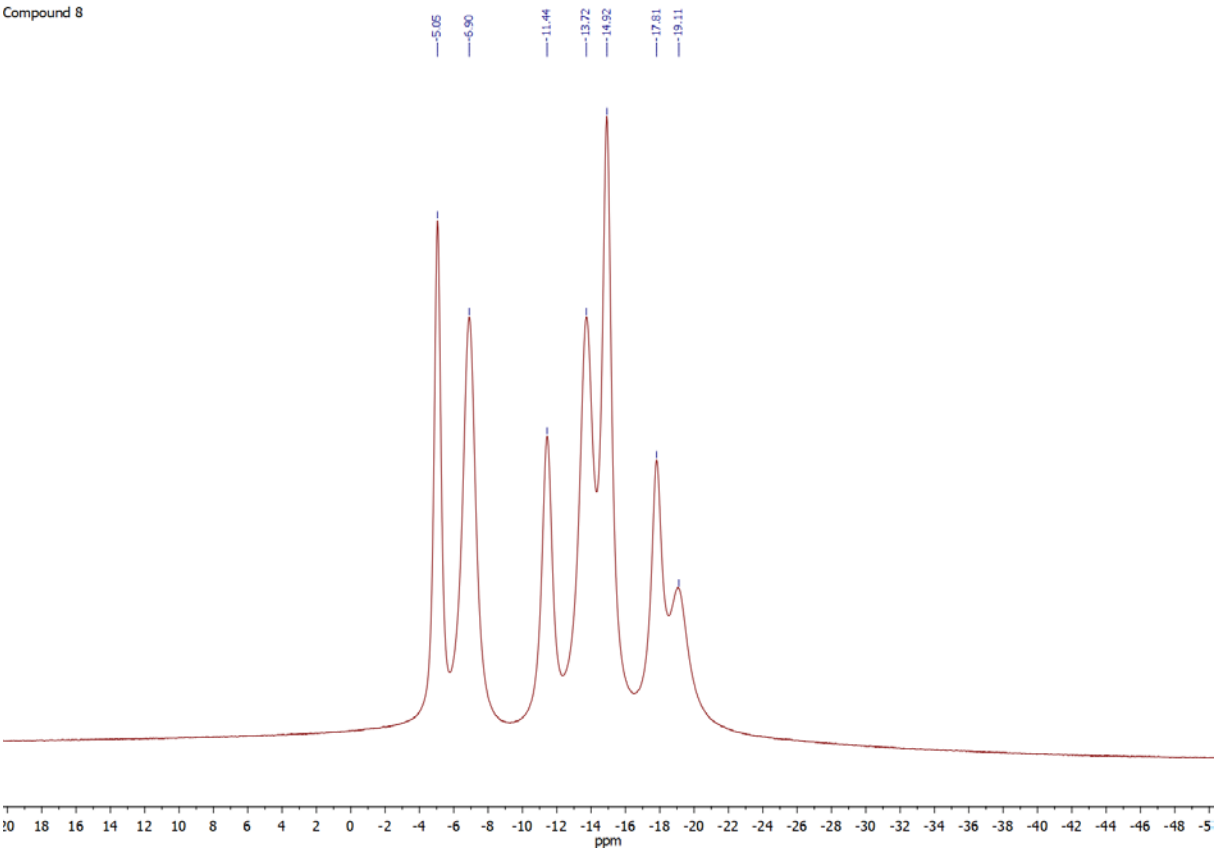


Figure S69: $^{11}B\{^{1}H\}$ NMR spectrum of compound **8**.

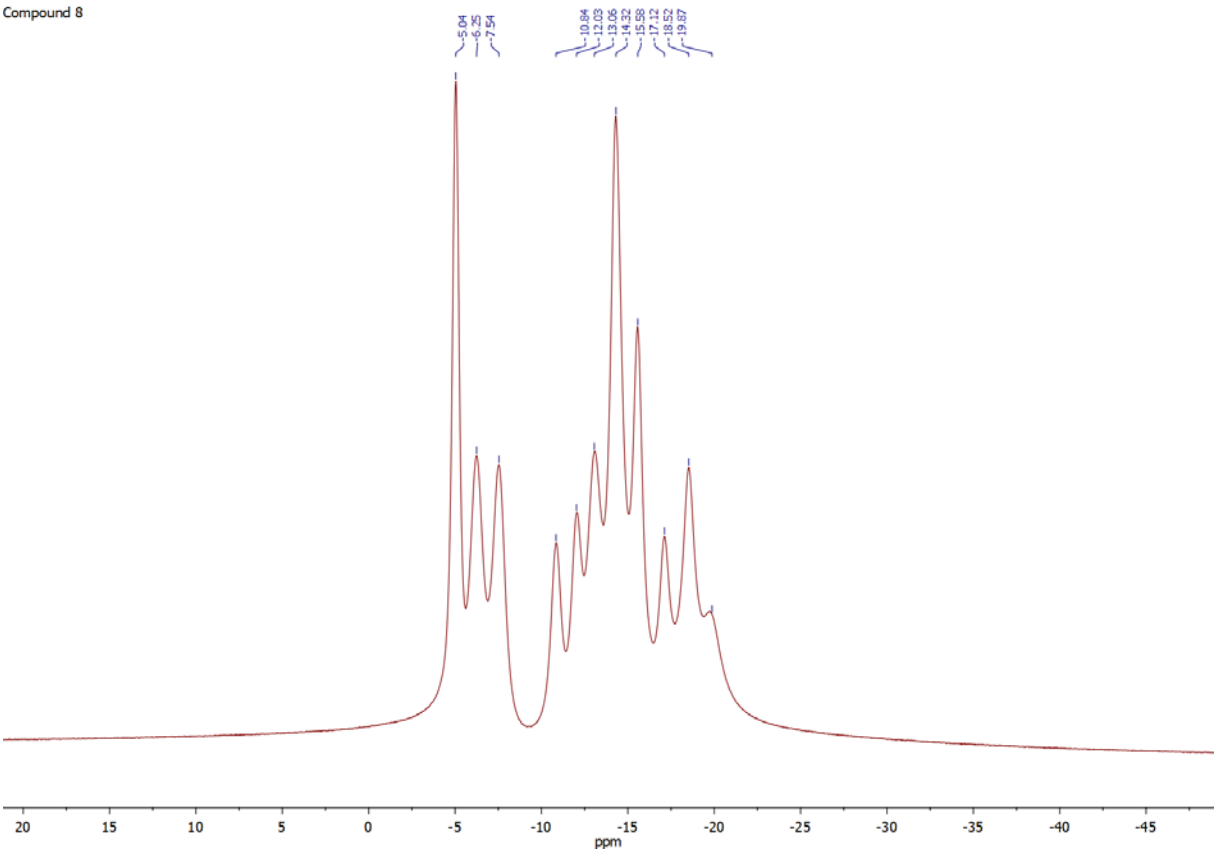


Figure S70: ^{11}B NMR spectrum of compound **8**.

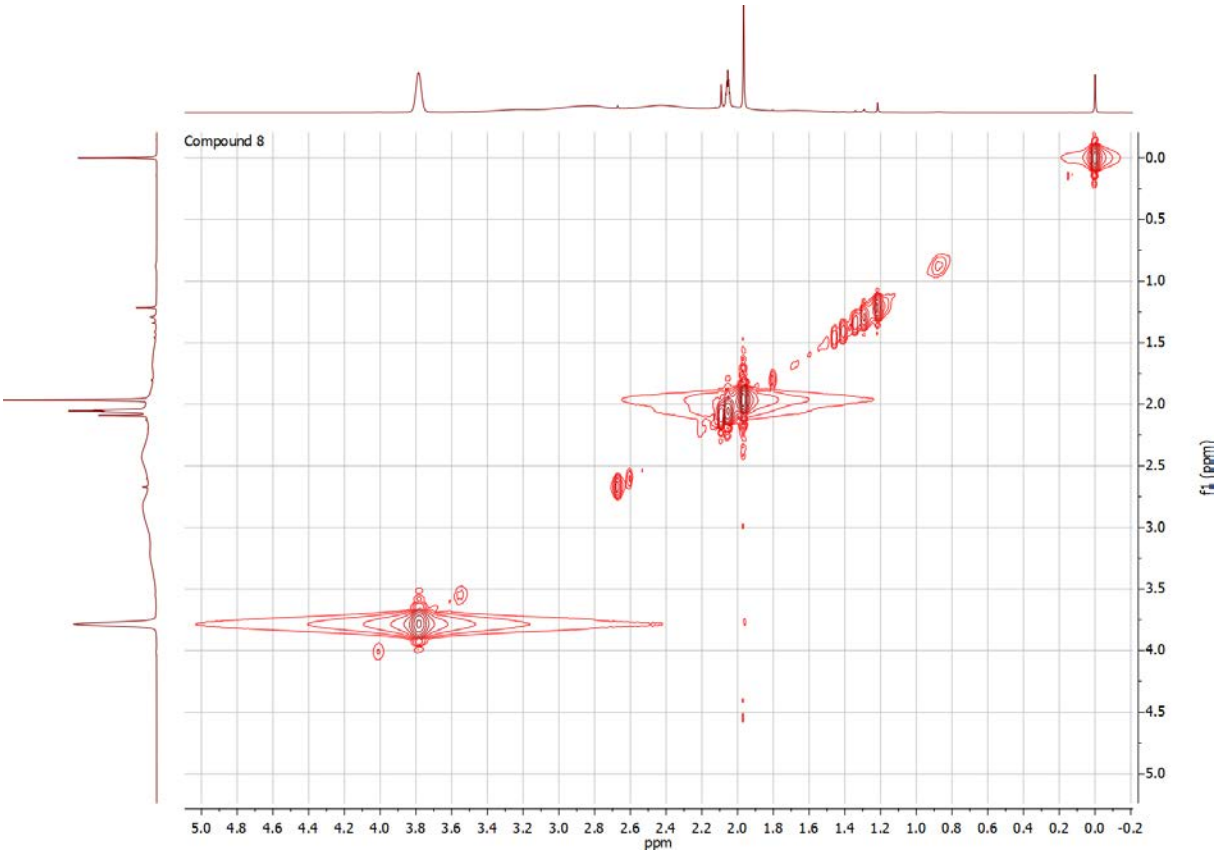


Figure S71: ^{1}H-^{1}H-COSY NMR spectrum of compound **8**.

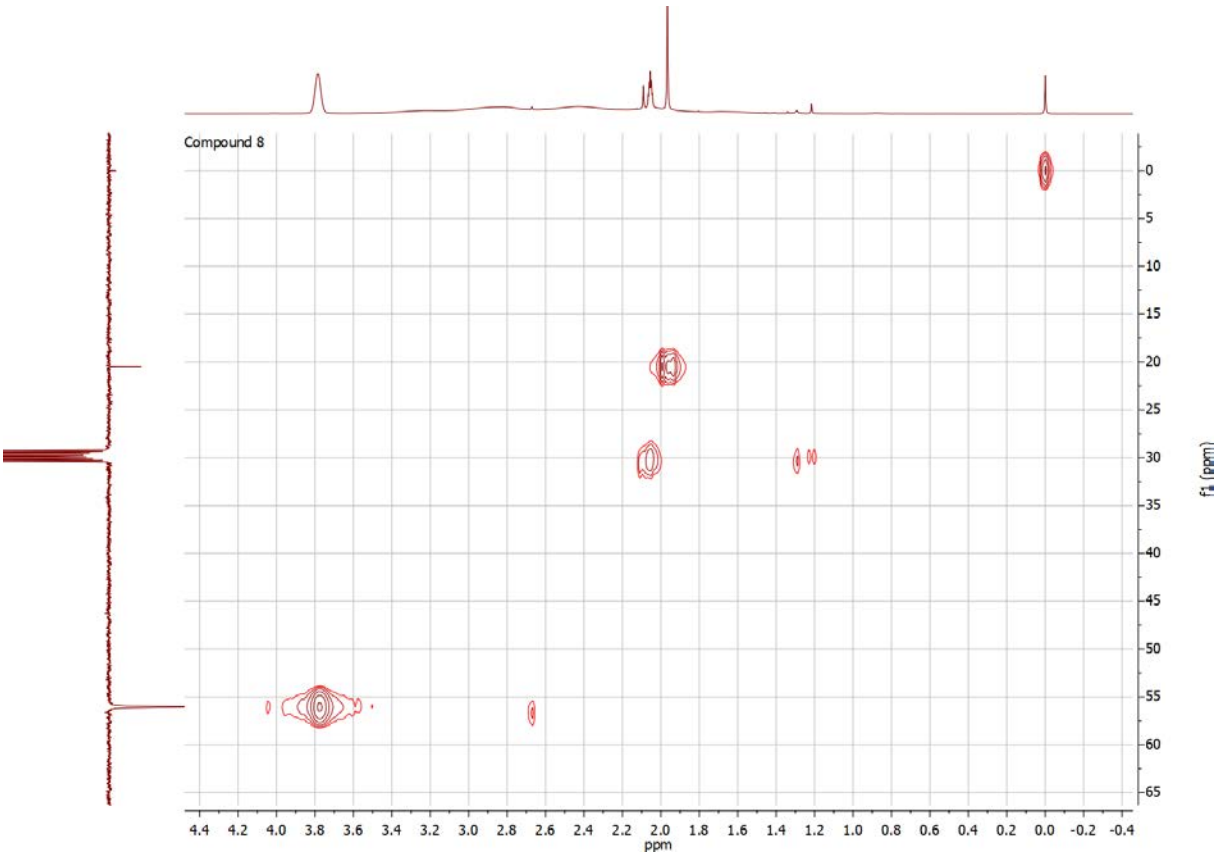


Figure S72: ^{1}H-^{13}C-HMQC NMR spectrum of compound **8**.

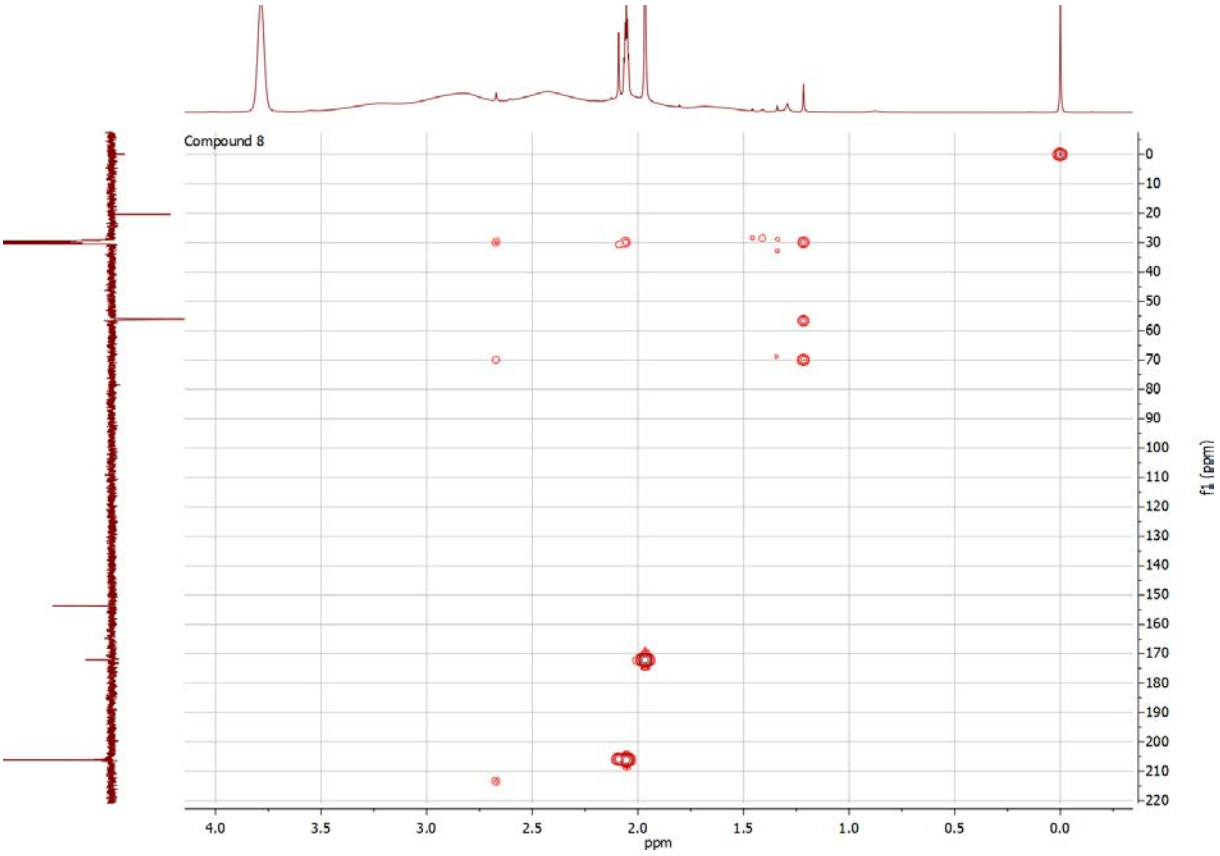


Figure S73: ^{1}H-^{13}C-HMBC NMR spectrum of compound **8**.

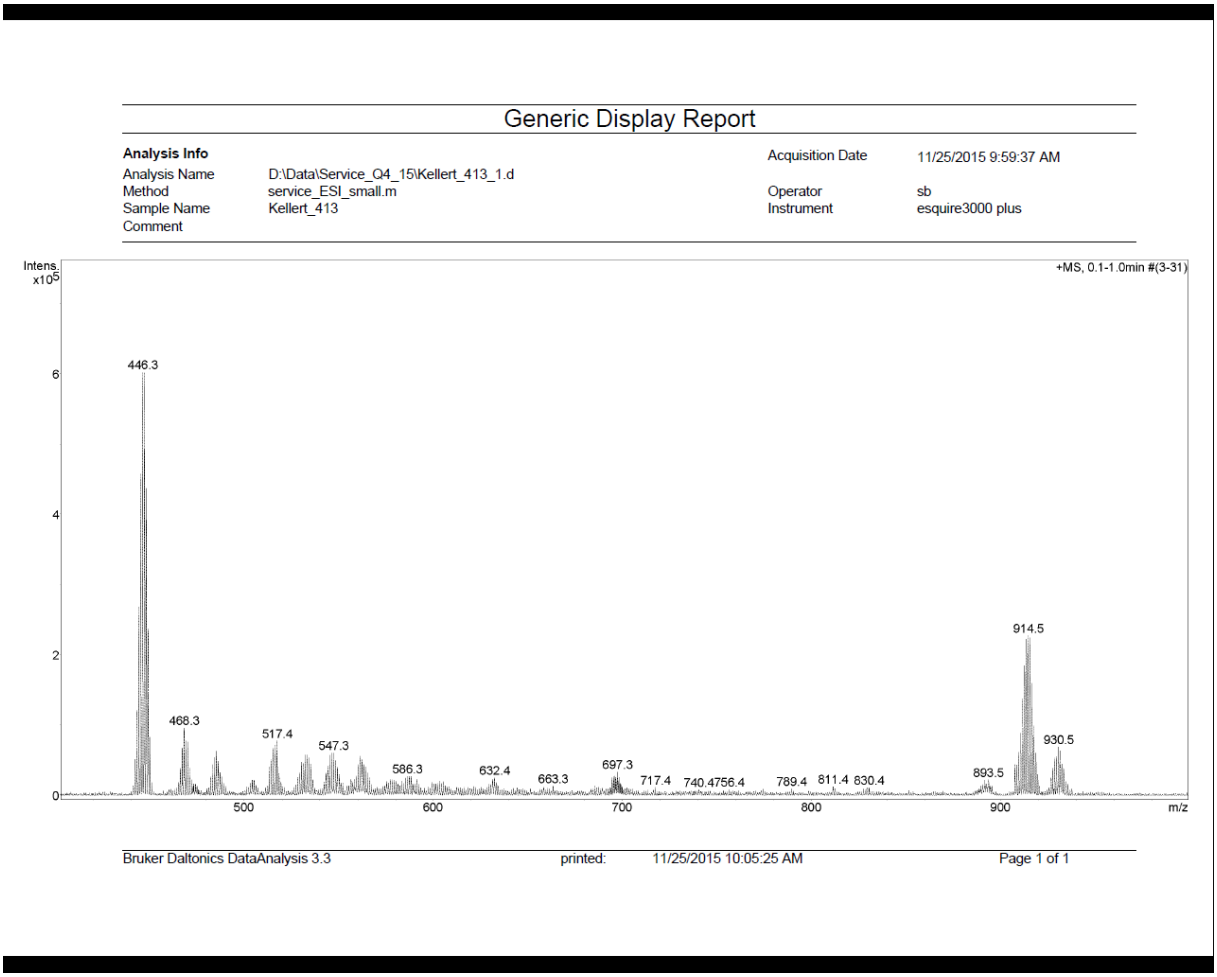


Figure S74: ESI MS of compound **8**.

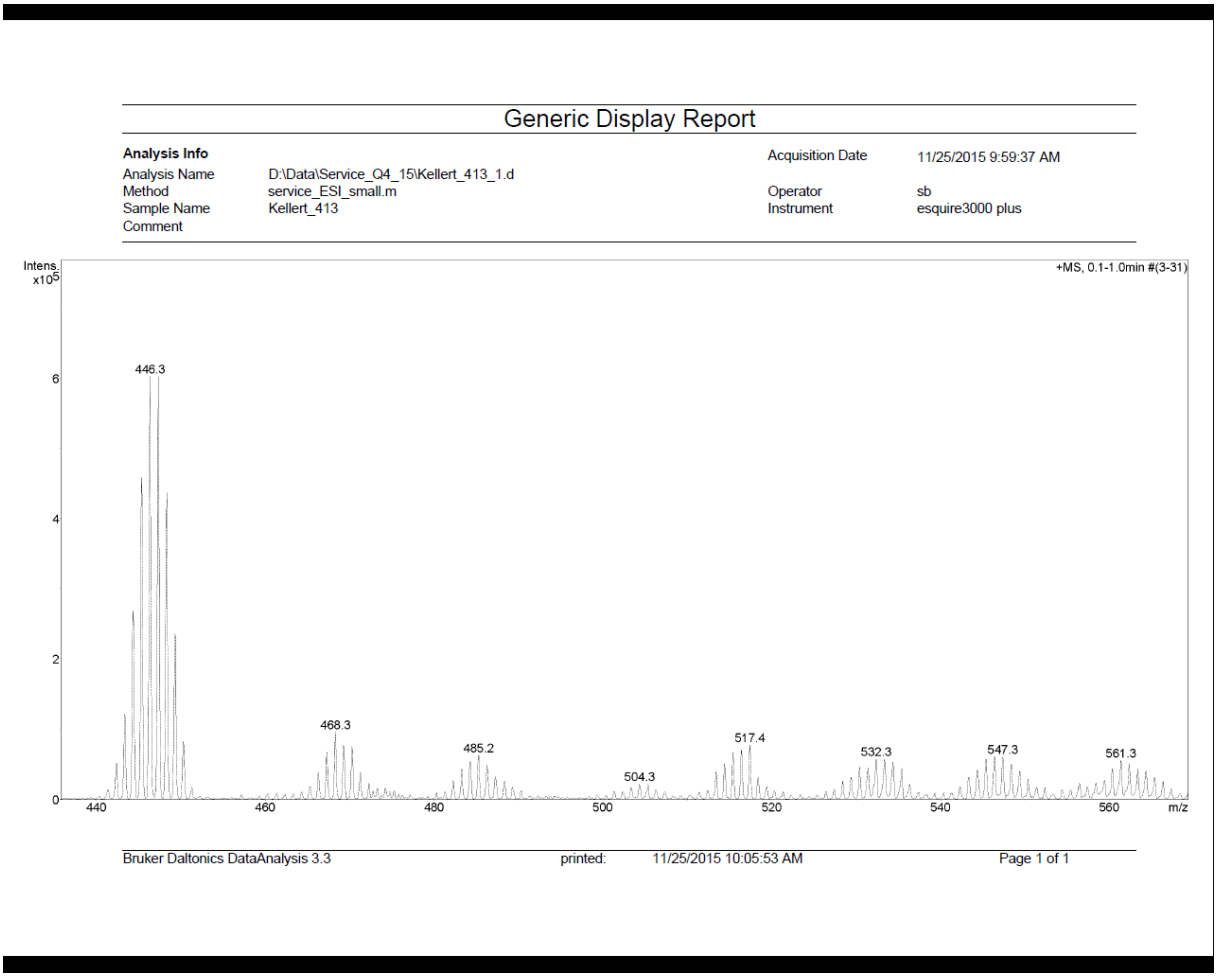


Figure S75: Section of the ESI MS of compound **8**.

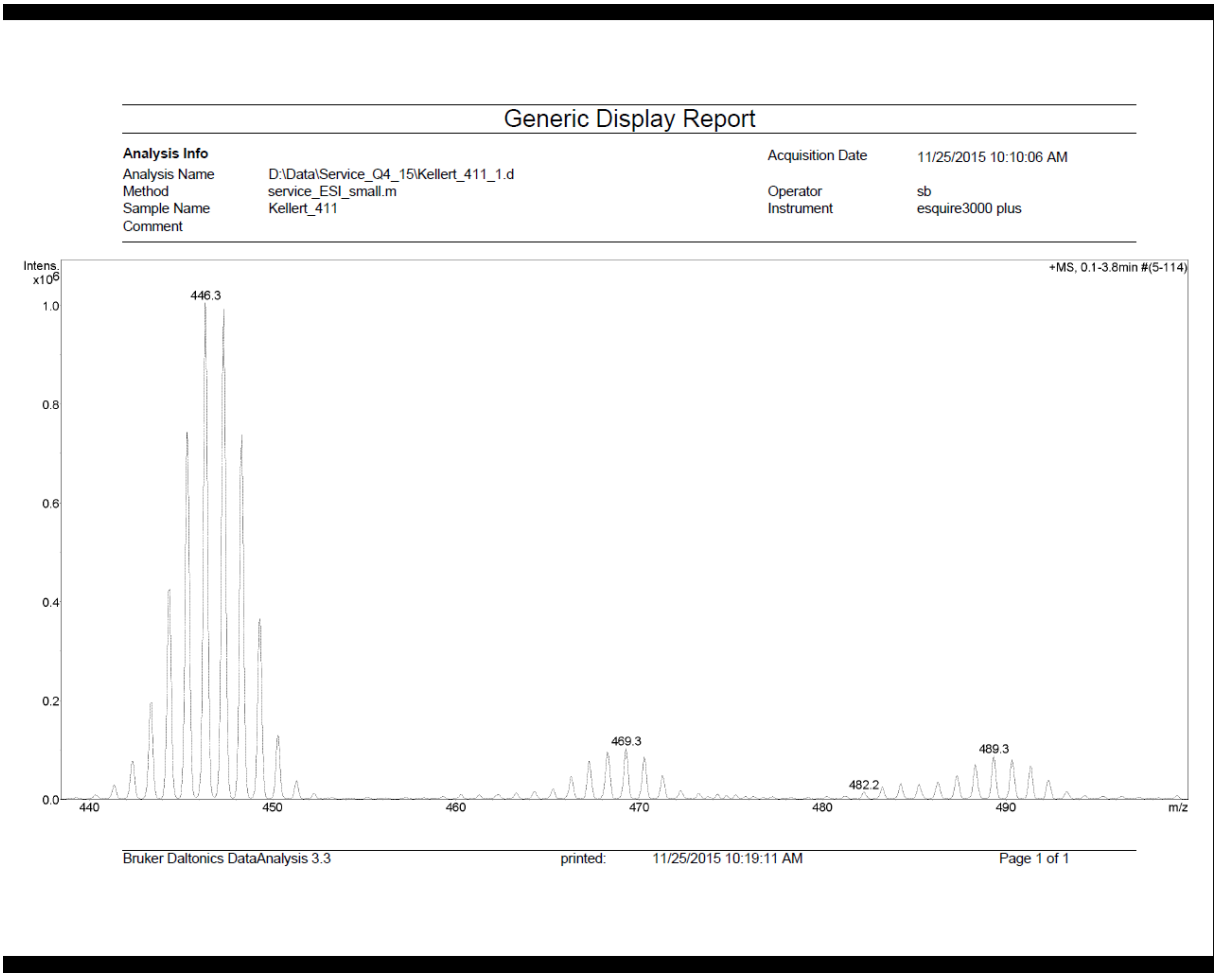


Figure S76: Section of the ESI MS of compound **8**.

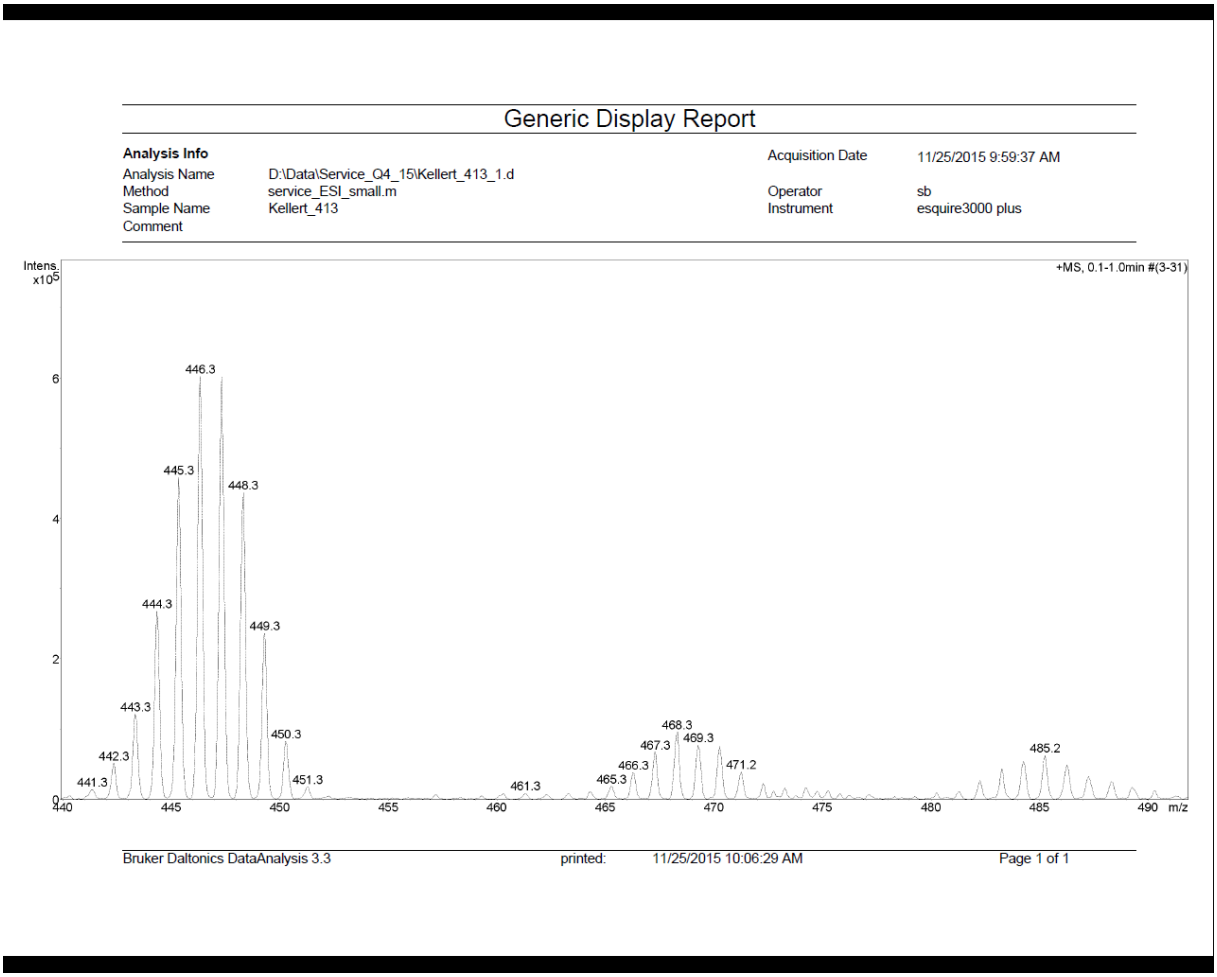


Figure S77: Section of the ESI MS of compound **8**.

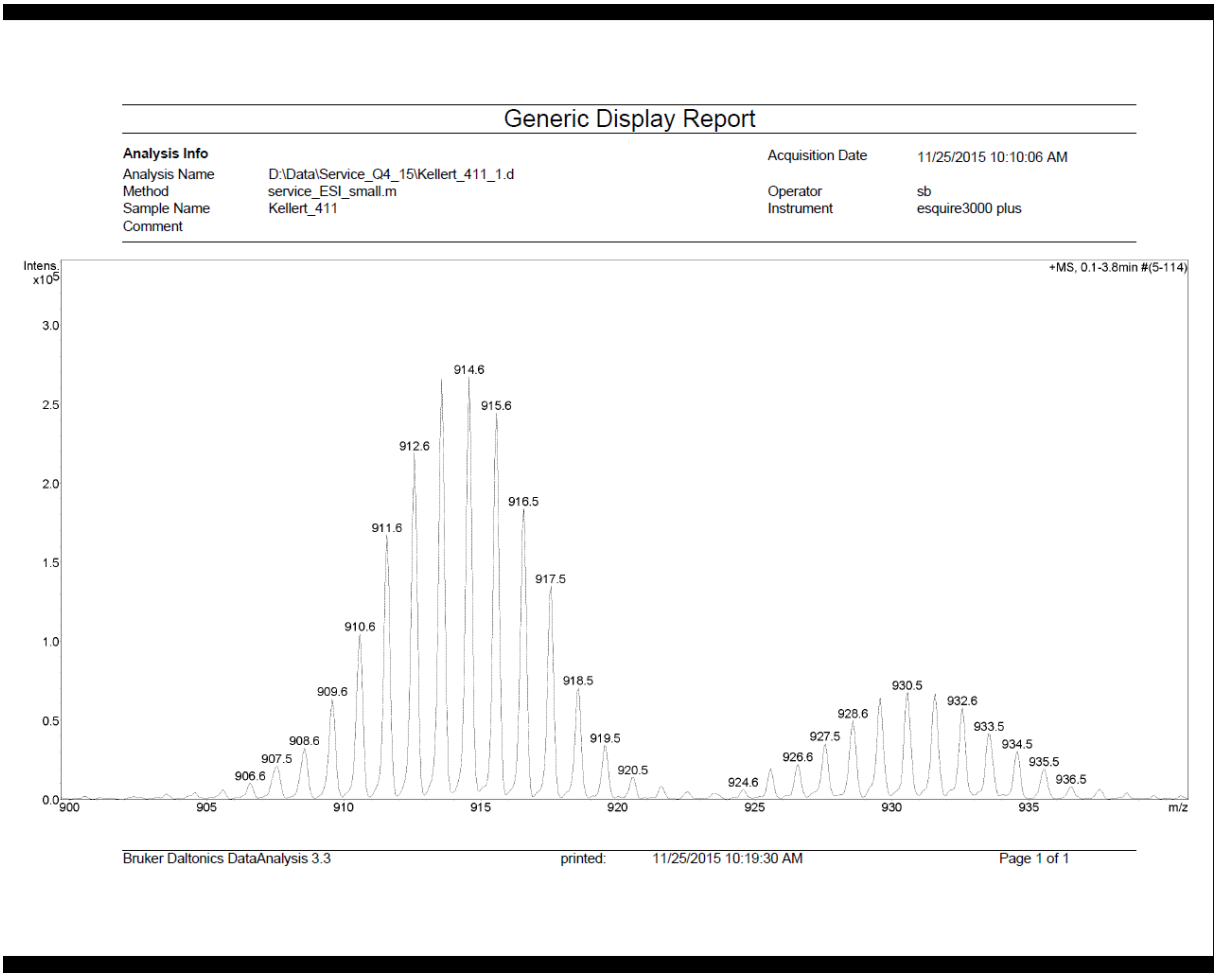


Figure S78: Section of the ESI MS of compound **8**.

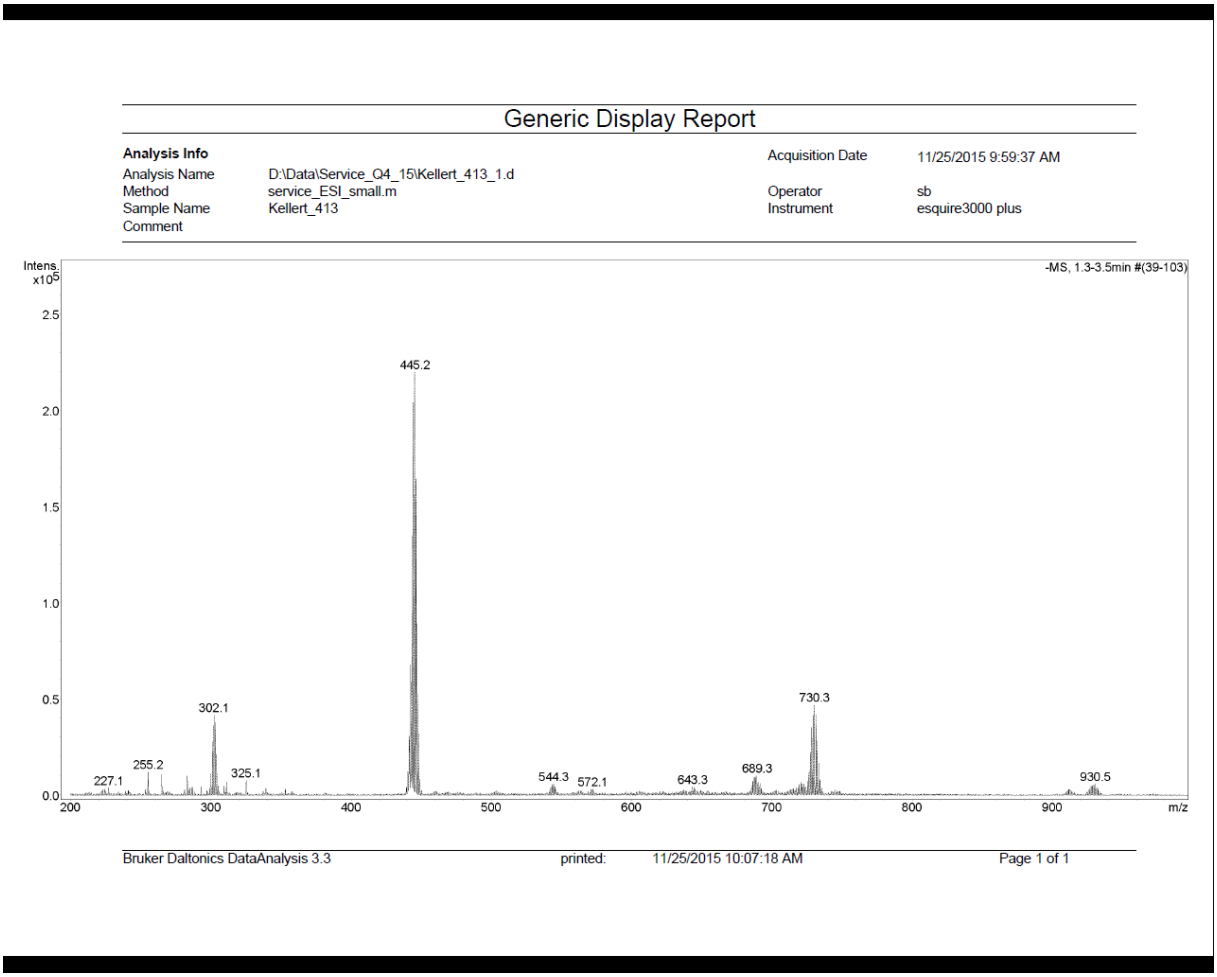


Figure S79: ESI MS (negative mode) of compound **8**.

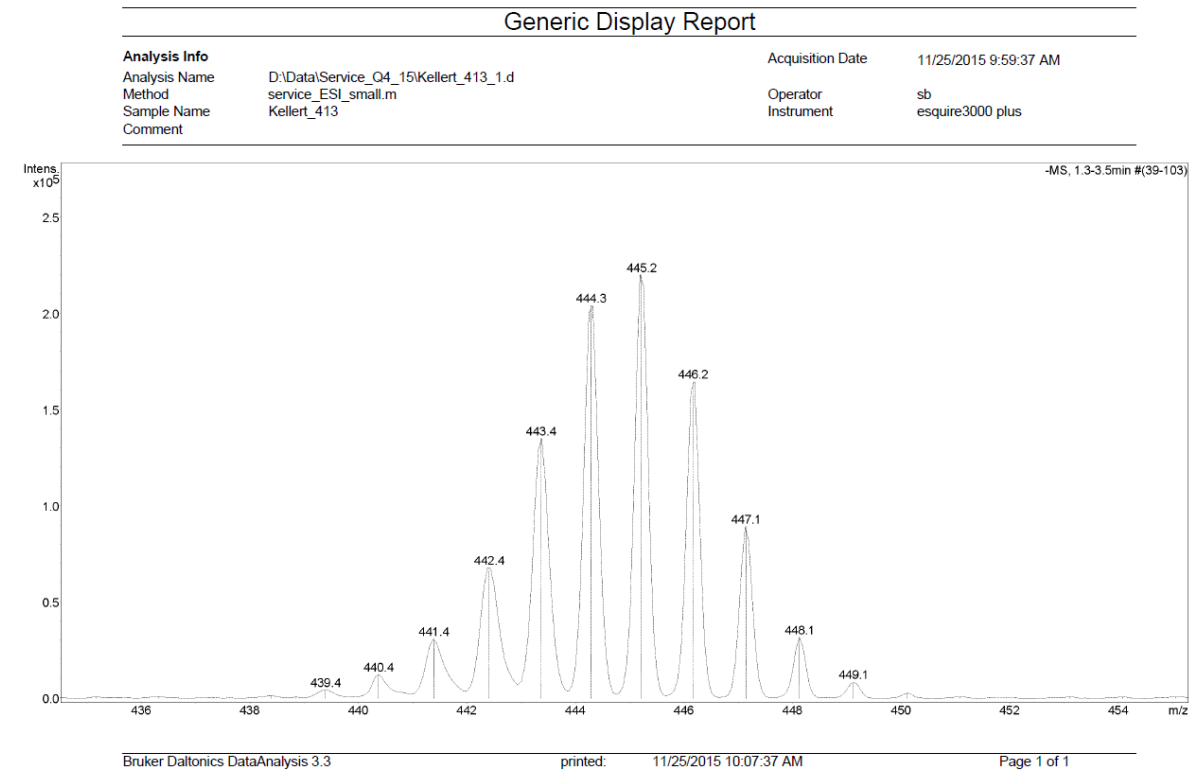


Figure S80: Section of the ESI MS of compound **8**.

Crystallographic data of 8

a) Single crystals obtained from acetone

Empirical formula	$C_{10}H_{29}B_{20}N_3O_2S_2$	
Formula weight	503.68	
Temperature	130(2) K	
Wavelength	71.073 pm	
Crystal system	Triclinic	
Space group	$P\bar{1}$	
Unit cell dimensions	a = 684.40(2) pm	α = 79.036(7)°
	b = 1151.9(1) pm	β = 86.920(4)°
	c = 1688.0(1) pm	γ = 87.857(5)°
Volume	1.3040(2) nm^3	
Z	2	
Density (calculated)	1.283 Mg/m^3	

Absorption coefficient	0.223 mm^{-1}
F(000)	516
Crystal size	0.2 x 0.1 x 0.05 mm^3
Theta range for data collection	1.981 to 27.692°
Index ranges	–8 ≤ h ≤ 8, –14 ≤ k ≤ 14, –21 ≤ l ≤ 21
Reflections collected	6900
Independent reflections	6900 [R(int) = 0.0317]
Completeness to theta = 25.350°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1 and 0.99008
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6900 / 30 / 450
Goodness-of-fit on F^2	0.776
Final R indices [I>2σ(I)]	R_1 = 0.0417, wR_2 = 0.0790
R indices (all data)	R_1 = 0.0987, wR_2 = 0.0874
Two-component twin	
Twin law by rows	1.00 0.00 0.00 0.11 –1.00 0.00 0.27 –0.01 –1.00
Twin domain ratio	0.881(3):0.119(3).
Residual electron density	0.284 and –0.272 e·$Å^{-3}$

Comments: Structure solution with SHELXT-2014 (dual-space method). Anisotropic refinement of all non-hydrogen atoms with SHELXL-2018. All H atoms were located on difference Fourier maps calculated at the final stage of the structure refinement. As a result of the twin refinement, the displacement parameter for H(11X) was not allowed to vary. Most of the second twin domain had been removed manually before the measurement by cutting the crystal. For intermolecular hydrogen donor-acceptor bonds see Table S3. The carborane C atoms could be identified and localised with a bond length and a displacement parameter analysis.

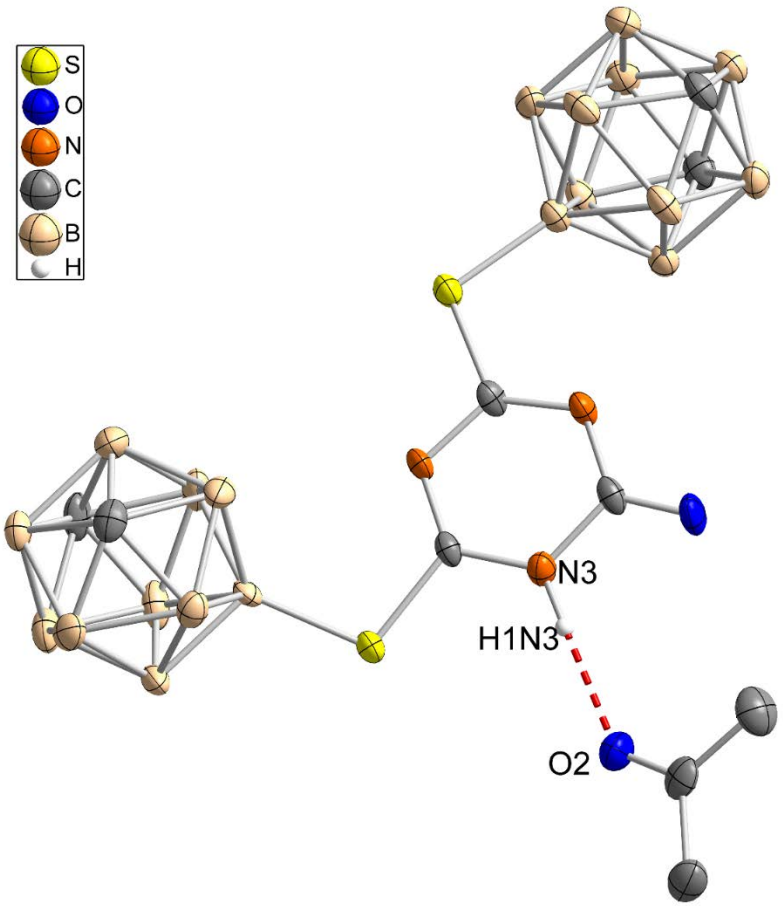


Figure S81: Molecular structure of **8**. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms are drawn with a fixed atom radius of 13.5 pm. Hydrogen atoms, which are not involved in hydrogen bonding, are omitted for clarity.

Table S3: Hydrogen bonds for **8** [pm and °].

D-H···A	d(D–H)	d(H···A)	d(D···A)	<(DHA)
N(3)–H(1N3)···O(2)	90(3)	196(3)	285.9(3)	177(3)

Symmetry transformations used to generate equivalent atoms: none; d = bond length or distance; < = bond angle; D = hydrogen bond donor atom; A = hydrogen bond acceptor atom.

b) Single crystals obtained from methanol

Empirical formula	$C_8H_{27}B_{20}N_3O_2S_2$
Formula weight	477.64
Temperature	130(2) K
Wavelength	71.073 pm
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	a = 687.59(3) pm α = 106.697(6)°
	b = 1595.78(9) pm β = 94.109(4)°
	c = 2381.8(2) pm γ = 96.237(4)°
Volume	2.4738(3) nm^3
Z	4
Density (calculated)	1.282 Mg/m^3
Absorption coefficient	0.231 mm^{-1}
F(000)	976
Crystal size	0.2 x 0.1 x 0.02 mm^3
Theta range for data collection	2.544 to 28.209°
Index ranges	$-9 \le h \le 8$, $-20 \le k \le 20$, $-29 \le l \le 29$
Reflections collected	18971
Independent reflections	10165 [R(int) = 0.0563]
Completeness to theta = 25.350°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1 and 0.99665
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10165 / 2 / 824
Goodness-of-fit on F^2	0.988
Final R indices [I>2σ(I)]	R_1 = 0.0686, wR_2 = 0.1423
R indices (all data)	R_1 = 0.1463, wR_2 = 0.1788
Residual electron density	0.559 and –0.436 $e \cdot Å^{-3}$

Comments: Structure solution with SHELXT-2014 (dual-space method). Anisotropic refinement of all non-hydrogen atoms with SHELXL-2018. Excluding solvent hydrogen atoms (methyl group), all other H atoms were located on difference Fourier maps calculated at the final stage of the structure refinement. The displacement parameter for H(1O3) is fixed. For

intermolecular hydrogen donor-acceptor bonds see Table S4 and Figure S82. The carborane C atoms are localised from a bond length and displacement parameter analysis.

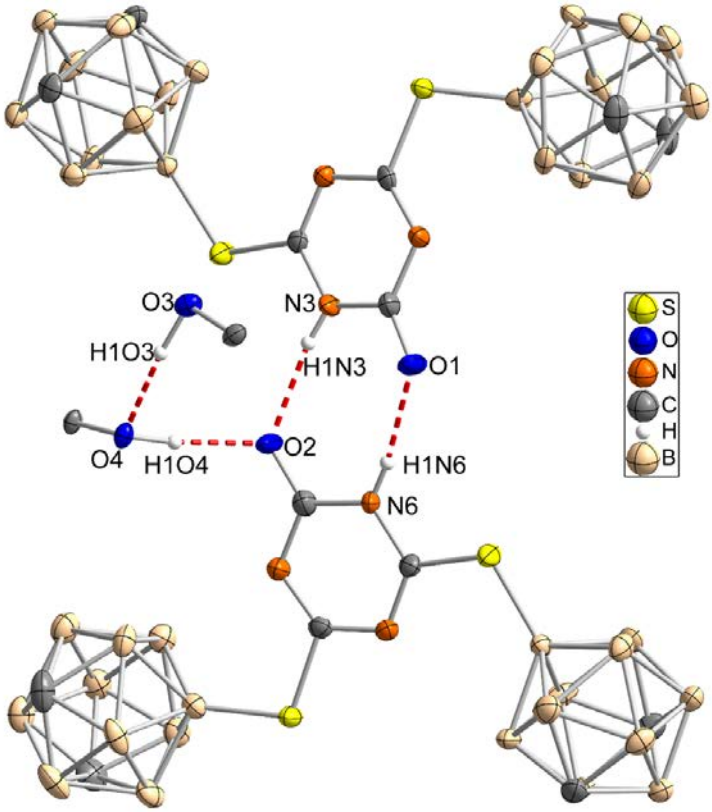


Figure S82: Molecular structure of **8**. Thermal ellipsoids are drawn at the 50% probability level, thermal ellipsoids of the solvent molecules at the 10% probability level. Hydrogen atoms are drawn with a fixed atom radius of 13.5 pm. Hydrogen atoms, which are not involved in hydrogen bonding, are omitted for clarity.

Table S4: Hydrogen bonds for **8** [pm and °].

D-H···A	d(D–H)	d(H···A)	d(D···A)	<(DHA)
N(3)–H(1N3)···O(2)	79(4)	197(4)	274.6(5)	170(4)
N(6)–H(1N6)···O(1)	83(4)	195(4)	277.6(5)	172(4)
O(3)–H(1O3)···O(4)	104.7(19)	186(2)	289.3(6)	169(4)
O(4)–H(1O4)···O(2)	97(2)	185(2)	281.7(4)	172(5)

Symmetry transformations used to generate equivalent atoms: none; d = bond length or distance; < = bond angle; D = hydrogen bond donor atom; A = hydrogen bond acceptor atom**.**

10. Peptide analytics: RP-HPLC and mass spectrometry

Table S5: Peptide conjugate nomenclature

Conjugate	Name
C1	NPY
C2	[F^{7},P^{34}]-NPY
C3	[K^{4}(**4'**),F^{7},P^{34}]-NPY
C4	[K^{4}(**4'**),F^{7},K^{18}(**4'**),P^{34}]-NPY
C5	[K^{4}(**4'**),F^{7},$K^{18,22}$(**4'**),P^{34}]-NPY

Column 1: Phenomenex Jupiter® 4u Proteo C12 90 Å (250 mm × 4.6 mm, 4 µm, 90 Å), flow rate: 0.6 mL/min

Column 2: Agilent VariTide RPC (250 mm × 4.6 mm, 6 µm, 200 Å), flow rate: 1.0 mL/min

Column 3: Phenomenex Aeris® Peptide 3.6u XB-C18 (250 mm × 4.6 mm, 3.6 µm, 100 Å), flow rate: 1.55 mL/min

Linear gradients: eluent A: 0.1 % (*v*/*v*) TFA in H_2O, eluent B: 0.08 % (*v*/*v*) TFA in ACN
Gradient A: 20 % to 70 % eluent B in A over 40 min
Gradient B: 30 % to 80 % eluent B in A over 40 min
Gradient C: 40 % to 90 % eluent B in A over 40 min

Table S6. Analysis of the prepared peptides by analytical RP-HPLC.

	HPLC analysis I				HPLC analysis II				
conjugate	**column**	**gradient**	**elution at %ACN**	**t_R [min]**	**column**	**gradient**	**elution at %ACN**	**t_R [min]**	**purity**
C1	1	A	46.6	21.3	3	A	40.3	16.2	> 95 %
C2	1	A	46.1	20.9	3	A	41.1	16.9	> 95 %
C3	1	B	52.8	18.2	2	B	57.0	21.6	> 95 %
C4	1	B	58.3	22.6	2	B	66.3	29.0	> 95 %
C5	1	C	64.9	19.9	2	C	72.5	26.0	> 95 %

Table S7. Analysis of the pure peptides by MALDI-ToF MS.

Conjugate	M_{exact} (calc.) [Da]	M_{exact} (exp.) $[M+H]^+$
C1	4251.1	4252.1
C2	4253.1	4254.1
C3	4758.4	4759.3
C4	5320.8	5321.9
C5	5867.1	5868.1

11. References

1 L. I. Zakharkin and I. V. Pisavera, *Phosphorus Sulfur*, 1984, **20**, 357–370.

2 a) J. Liu, E. Rühl, A. P. Hitchcock, D. N. McIlroy, J. D. Bozek, T. Tyliszczak, A. Knop-Gericke, N. M. Boag and P. A. Dowben, *Z. Phys. Chem.*, 2014, **228**; b) V. I. Bregadze, *Chem. Rev.*, 1992, **92**, 209–223; c) A. M. Spokoyny, C. D. Lewis, G. Teverovskiy and S. L. Buchwald, *Organometallics*, 2012, **31**, 8478–8481; d) V. N. Kalinin and V. A. Ol'shevskaya, *Russ. Chem. B.*, 2008, **57**, 815–836.

3 F. Neese, *WIREs Comput. Mol. Sci.*, 2012, **2**, 73–78.

4 a) J. Tao, J. P. Perdew, V. N. Staroverov and G. E. Scuseria, *Phys. Rev. Lett.*, 2003, **91**, 146401; b) V. N. Staroverov, G. E. Scuseria, J. Tao and J. P. Perdew, *J. Chem. Phys.*, 2003, **119**, 12129–12137.

5 a) A. Schäfer, H. Horn and R. Ahlrichs, *J. Chem. Phys.*, 1992, **97**, 2571–2577; b) F. Weigend and R. Ahlrichs, *Phys. Chem. Chem. Phys.*, 2005, **7**, 3297–3305; c) F. Weigend, *Phys. Chem. Chem. Phys.*, 2006, **8**, 1057–1065.

6 a) K. Eichkorn, F. Weigend, O. Treutler and R. Ahlrichs, *Theor. Chem. Acc.*, 1997, **97**, 119–124; b) K. Eichkorn, O. Treutler, H. Öhm, M. Häser and R. Ahlrichs, *Chem. Phys. Lett.*, 1995, **240**, 283–290.

7 E. F. Pettersen, T. D. Goddard, C. C. Huang, G. S. Couch, D. M. Greenblatt, E. C. Meng and T. E. Ferrin, *J. Comput. Chem.*, 2004, **25**, 1605–1612.

8 a) S. Saure, *Chem. Ber.*, 1950, 335–340; b) P. Rys, A. Schmitz and H. Zollinger, *Helv. Chim. Acta*, 1971, **54**, 163–176; c) Z. Yan, W.-L. Xue, Z.-X. Zeng and M.-R. Gu, *Ind. Eng. Chem. Res.*, 2008, **47**, 5318–5322; d) R. Bacaloglu and J. Havlik, *J. Prakt. Chem.*, 1983, **325**, 309–318; e) S. Horrobin, *J. Chem. Soc.*, 1963, 4130–4145; f) K. Matsui and A. Sakamoto, *Yuki Gosei Kagaku Kyokaishi*, 1960, **18**, 175–183.

9 a) A. Khalil, K. Ishita, T. Ali and W. Tjarks, *Future Med. Chem.*, 2013, **5**, 677–692; b) M. Misiak, F. Mantegazza and G. L. Beretta, *Curr. Pharm. Design*, 2016, **22**, 6596–6611; c) M. Sirajuddin, S. Ali and A. Badshah, *J. Photoch. Photobio. B*, 2013, **124**, 1–19.